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RhCl3/amine-catalyzed [2+2+2] cyclization of alkynes

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Graphical Abstract

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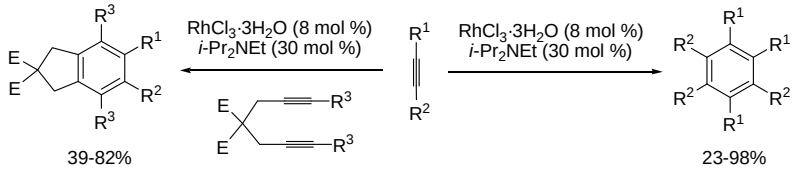

39-82% 23-98%

$RhCl_3$/amine-catalyzed [2+2+2] cyclization of alkynes

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Abstract—The $RhCl_3$•$3H_2O$/*i*-Pr_2NEt-catalyzed [2+2+2] cyclotrimerization of alkynes has been achieved. The reaction can be widely used for various alkynes and provides tri- or hexa-substituted benzenes regioselectively in high yields. The [2+2+2] cycloaddition of diynes and alkynes is also developed, and it affords benzene derivatives in moderate to high yields.

Keywords: Rh/amine catalyst; Cyclotrimerization; Hexa-substituted benzene.

1. Introduction

The transition metal-catalyzed [2+2+2] cyclotrimerization of alkynes has been well known as a useful method for the construction of hexa-substituted benzenes in a one-step.[1–9] Since the first discovery by Reppe and co-workers,[10] various transition metals (Ni,[2] Rh,[3] Pd,[4] Ru,[5] Co,[6] Ti,[7] and Mo[8]) catalyzed [2+2+2] cycloadditions have been found to date. However, it has been difficult to cyclize sterically hindered alkynes in a highly efficient and highly regioselective manner. For instance, the efficiency of the trimerization of internal alkynes bearing aryl and ester moieties, such as alkyl phenylpropiolate (PhC≡CCO_2R), is quite low.[9] Therefore, a more general and efficient catalyst has been in great demand. In recent years, amine ligands have received considerable attention for their unique reactivity.[11] For instance, Vicic and co-workers reported the $Ni(cod)_2$/*tert*-butylterpyridine-catalyzed cross-coupling reaction of alkyl zinc bromide and alkyl iodide.[11d] The ligand system could catalyze Negishi couplings at room temperature in an amide-free solvent. Okamoto and co-workers reported that the $CoCl_2$•$6H_2O$/2-iminomethylpyridine-catalyzed cycloaddition of diynes and alkynes proceeded efficiently.[11c] The catalytic effect was specific to reactions with the 2-aminomethylpyridine ligand and no effect was observed with phosphine ligands. The reactivities in these reactions are quite different from those in metal/phosphine ligand chemistry. These results led us to investigate the transition metal/amine ligand-catalyzed trimerization of internal alkynes. Recently, we performed the $RhCl_3$•$3H_2O$/amine-catalyzed cyclization of alkynes, which can be widely used for internal alkynes.[12] The cyclization of alkynes or diynes and alkynes proceeded smoothly to afford multi-substituted benzenes regioselectively in moderate to high yields.

2. Results and Discussions

The $RhCl_3$•$3H_2O$-catalyzed cyclotrimerization of internal alkynes was performed successfully by the addition of a catalytic amount of an electron-rich and bulky alkylamine. First, using ethyl phenylpropiolate (**1a**) as a model substrate, the effect of the additives in the cyclotrimerization was investigated (Table 1). In the absence of amine, $RhCl_3$•$3H_2O$ catalyzed the cyclotrimerization of alkyne **1a** to give cyclized product **2a** in only 20% yield (entry 1). On the other hand, the trimerization of alkyne **1a** was efficiently promoted by the addition of *tert*-amines. In the presence of Et_3N, which is a frequently used base, the yield of the products increased to 67% (entry 2). To compare the effect of Et_3N with that of other amines, we examined the cyclotrimerization of alkyne **1a** using various electron-rich amines (entries 3–6). The trimerization of alkyne **1a** using *i*-Pr_2NEt, Me_3SiNEt_2, and dicyclohexylmethylamine (Cy_2NMe), gave cycloadducts **2a** and **3a** in respective yields of 91, 80, and 75% (entries 3–5). Only in the case of $N(C_2H_4)_3N$ was the yield of products **2a** and **3a** significantly reduced (24%, entry 6). These facts indicate that the reactivity would be influenced by the bulkiness of the *tert*-amines. Indeed, the yields of cyclized products **2a** and **3a** increased with an increase in the

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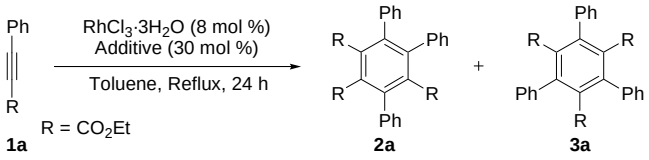
bulkiness of the amines: *i*-Pr_2NEt (91%) > Et_3N (67%) > $N(C_2H_4)_3N$ (24%). Next, the cyclotrimerization of **1a** using $PhNMe_2$ and Ph_3N, the yields of cycloadducts **2a** and **3a** dramatically decreased (entries 7 and 8). These results suggest that such electron-deficient amines are not effective in cyclotrimerization. Pyridine was not effective, and starting material **1a** was recovered quantitatively, probably due to the generation of $RhCl_3(py)_3$, which might not be an active catalyst for the reaction (entry 9).[13] In a similar manner, the $RhCl_3$•$3H_2O$-catalyzed cyclotrimerization was performed with *sec*- and *prim*-amines, affording cycloadducts **2a** and **3a** in yields of 17–69% (entries 10–12). Among the examined *sec*- and *prim*-amines, electron-rich and bulky amines, *e.g.*, *i*-Pr_2NH, were the most effective (entry 10). Bidentate amines such as TMEDA (*N*,*N*,*N*′,*N*′-tetramethylethylenediamine) and 2,2′-bipyridyl were not effective at all (entries 13 and 14). Interestingly, commonly used phosphine ligands were not effective for the cyclotrimerization (entries 15–20). With alkyl phosphines, the yields of cyclized products **2a** and **3a** were lower than 6% (entries 15–17). PPh_3 and bidentate phosphines were not effective at all (entries 18–20). Above all, it has been found that the presence of an electron-rich and bulky amine is essential for the cyclotrimerization reaction. In particular, $RhCl_3$•$3H_2O$/*i*-Pr_2NEt is the best combination for promoting the cyclotrimerization of alkyne **1a**, probably due to the generation of an "active catalyst" *in situ*.

Table 1

Cyclotrimerization using several additives



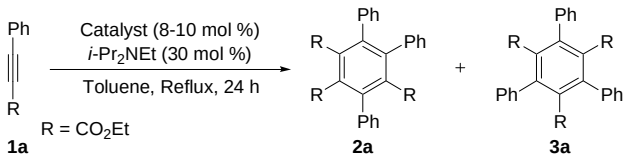
Entry	Additive	Yield of **2a**+**3a** (%)[a]	**2a**:**3a**[b]
1	None	20	99:1
2	Et_3N	67	98:2
3	*i*-Pr_2NEt	91	96:4
4	Cy_2NMe	80	96:4
5	Me_3SiNEt_2	75	97:3
6	$N(C_2H_4)_3N$	24	95:5
7	$PhNMe_2$	45	96:4
8	Ph_3N	26	97:3
9	Pyridine	-	-
10	*i*-Pr_2NH	69	95:5
11	Et_2NH	32	97:3
12	*t*-$BuNH_2$	17	95:5
13	TMEDA	-	-
14	2,2′-Bipyridyl	-	-
15	PBu_3	6	73:27
16	P(*t*-Bu)$_3$	5	90:10
17	PCy_3	<1	-
18	PPh_3	-	-
19	Dppp	<1	93:7
20	*(S)*-BINAP	-	-

[a] Isolated yield. [b] Determined by ^1H NMR.

To evaluate the catalytic activity of $RhCl_3$•$3H_2O$, several transition metal catalysts were used for the cyclotrimerization of ethyl phenylpropiolate (**1a**) (Table 2). First, other Rh(III) catalysts were employed for the reaction (entries 1 and 2). $RhCl_3$ (anhydrous) exhibited an activity similar to that of $RhCl_3$•$3H_2O$, affording cyclized products **2a** and **3a** in yields of 89% and resulting in high product selectivity (**2a**:**3a** = 99:1) (entry 1). This fact suggested that the presence of a small amount of water might not affect the reaction. On the other hand, $Rh(acac)_3$ (acac = acetylacetonate) was not effective (entry 2), resulting in the formation of only 6% yields of cyclized products **2a** and **3a**. $[Rh(OAc)_2]_2$, a Rh(II) catalyst, also showed poor catalytic activity to afford 11% yields of cyclized products **2a** and **3a** (entry 3). Next, Rh(I) catalysts were utilized for the trimerization of **1a** (entries 4–7). Among the Rh(I) catalysts examined thus far, no catalyst showed higher activity and higher regioselectivity than $RhCl_3$•$3H_2O$. Cationic Rh(I) complexes have received great attention as useful catalysts for cycloadditions. The reaction of alkyne **1a** with $[Rh(cod)_2][BF_4]$ (cod = 1,5-cyclooctadiene) gave moderate yields of cyclized products **2a** and **3a**, but exhibited poor regioselectivity less than that with $RhCl_3$•$3H_2O$ (**2a**:**3a** = 69:31) (entry 4). Using neutral Rh(I) catalysts such as $[RhCl(cod)]_2$, $RhCl(PPh_3)_3$, and Rh(acac)(cod), the yields and the regioselectivities of the cyclized products decreased significantly (entries 5–7). Notably, the reaction catalyzed by $RhCl(PPh_3)_3$, which is one of the typical catalysts for the trimerization reaction, gave the cyclized products in a yield of 60% and in the ratio of 62:38 (**2a**:**3a** = 37%:23%) (entry 6). Several other metal catalysts were also employed in the reaction. The trimerization of alkyne **1a** using $PdCl_2$, $PtCl_2$, and $IrCl_3$ gave cycloadducts **2a** and **3a** in respective yields of a trace, 10%, and 3% (entries 8–10). With other metal halides, such as $CoCl_2$, $CoCl_2$•$3H_2O$, $NiCl_2$, $RuCl_3$•nH_2O, $CrCl_2$, $CrCl_3$, $FeCl_3$•$6H_2O$, CuCl, $CuCl_2$•$2H_2O$, $SmCl_3$, $TiCl_4$, $ZnCl_2$, $PbCl_2$, and $BiCl_3$, cyclized products **2a** and **3a** were not obtained at all. Above all, among thus far examined catalysts, the most effective catalyst is $RhCl_3$•$3H_2O$/*i*-Pr_2NEt which can promote the cyclotrimerization efficiently in a virtually complete regioselective manner.

Table 2

Cyclotrimerization using several catalysts[a]



Entry	Catalyst	Yield of **2a**+**3a** (%)[b]	**2a**:**3a**[c]
1	$RhCl_3$	89	99:1
2	$Rh(acac)_3$	6	93:7
3	$[Rh(OAc)_2]_2$	11	93:7
4	$[Rh(cod)_2][BF_4]$	81	69:31
5	$[RhCl(cod)]_2$	63	87:13
6	$RhCl(PPh_3)_3$	60	62:38
7	Rh(acac)(cod)	29	85:15

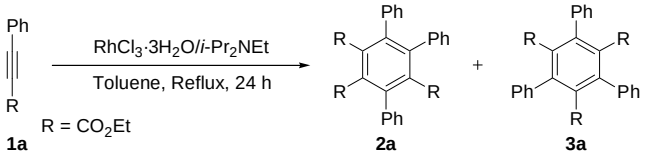
8	$PdCl_2$	<1	-
9	$PtCl_2$	10	86:14
10	$IrCl_3$	3	55:45

[a] Inactive catalysts: $CoCl_2$, $CoCl_2•3H_2O$, $NiCl_2$, $RuCl_3•nH_2O$, $CrCl_2$, $CrCl_3$, $FeCl_3•6H_2O$, CuCl, $CuCl_2•2H_2O$, $SmCl_3$, $TiCl_4$, $ZnCl_2$, $PbCl_2$, $BiCl_3$.
[b] Isolated yield. [c] Determined by ^{1}H NMR.

The reaction efficiency of the $RhCl_3•3H_2O$/*i*-Pr_2NEt-catalyzed cyclization of **1a** was highly influenced by the amounts and the ratio of $RhCl_3•3H_2O$ and *i*-Pr_2NEt (Table 3). In the presence of $RhCl_3•3H_2O$ (8 mol %) and *i*-Pr_2NEt (30 mol %), the cyclotrimerization of alkyne **1a** occurred smoothly to give products **2a** and **3a** in 91% yield (entry 1). The ratio of the amount of $RhCl_3•3H_2O$ to that of *i*-Pr_2NEt significantly affected the product yield (entries 2–5), and the best yields of cycloadducts **2a** and **3a** were obtained with a 1:3 mixture of $RhCl_3•3H_2O$ and *i*-Pr_2NEt (entry 3). When the amount of $RhCl_3•3H_2O$ was decreased to 2 mol % and 1 mol %, the yields of products **2a** and **3a** decreased to 71% and 57% yield, respectively (entries 6 and 7). From these results, it was found that the cyclotrimerization of **1a** required approximately 3 equivalents of *i*-Pr_2NEt in comparison to $RhCl_3•3H_2O$, and the yields of products **2a** and **3a** decreased with an increase or decrease in the amount of *i*-Pr_2NEt. With 3 mol % $RhCl_3•3H_2O$ and 9 mol % of the *i*-Pr_2NEt catalyst, cycloadducts **2a** and **3a** were obtained in the highest yield (93%).

Table 3

Effects of the amounts and the ratio of $RhCl_3•3H_2O$/*i*-Pr_2NEt



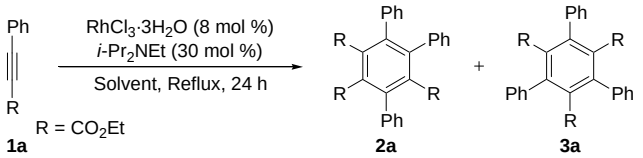
Entry	$RhCl_3•3H_2O$ (mol %)	*i*-Pr_2NEt (mol %)	Yield of **2a**+**3a** (%)[a]	**2a**:**3a**[b]
1	8	30	91	96:4
2	3	12	84	96:4
3	3	9	93	97:3
4	3	6	74	96:4
5	3	3	52	95:5
6	2	6	71	95:5
7	1	3	57	95:5

[a] Isolated yield. [b] Determined by ^{1}H NMR.

The effect of the solvent on the cyclotrimerization was investigated. In several solvents, the $RhCl_3•3H_2O$/*i*-Pr_2NEt-catalyzed cyclotrimerization of **1a** was performed at reflux (Table 4). In toluene, the cyclotrimerization of alkyne **1a** afforded cycloadducts **2a** and **3a** in 91% yields in the ratio of 96:4 (entry 1). Other aromatic hydrocarbon such as *o*-xylene and benzene were used for the reaction, resulting in a decrease in the yields of adducts **2a** and **3a** (87% and 67%) (entries 2 and 3). Ethers could also be used for the reaction. When the reaction was carried out in DME (1,2-dimethoxyethane) or 1,4-dioxane, cycloadducts **2a** and **3a** were obtained in yields of 87 and 83%, respectively (entries 4 and 5). In THF, the yields of products **2a** and **3a** dramatically decreased to 47% (entry 6). Et_2O was not of any use, and most of starting material **1a** was recovered (entry 7). These facts indicated that the yields of cyclotrimerization products **2a** and **3a** could be affected by the reaction temperature (refluxing temperature of the solvents). Indeed, the yields of the cyclized products increased with an increase in the reaction temperature: *o*-xylene (144 °C), toluene (111 °C), 1,4-dioxane (101 °C), or DME (83 °C) > benzene (80 °C) > THF (66 °C) > Et_2O (35 °C). Alcohols could be also utilized in the trimerization of alkyne **1a** (entries 8 and 9). The cyclotrimerization of **1a** in *i*-PrOH afforded products **2a** and **3a** in 86% yield, while the regioselectivity was lower than that in toluene (**2a**:**3a** = 85:15) (entry 8). In other solvents, such as CH_3CN, H_2O, 1,2-dichloroethane and CH_2Cl_2, similar cyclotrimerization occurred to afford 18–59% yields of adducts **2a** and **3a** in the ratio of 72:28–89:11 (entries 10–13). Alkanes, *e.g.*, hexane and heptane, were not of any use; thus, most of starting material **1a** was recovered (entries 14 and 15). Above all, it was found that several kinds of solvents could be used and the best choice of the solvent is toluene, in which, the best yields and highest regioselectivity could be attained (91%, **2a**:**3a** = 96:4). Thus, $RhCl_3•3H_2O$/*i*-Pr_2NEt/toluene is the best combination for promoting the cyclotrimerization of alkyne **1a**.

Table 4

Cyclotrimerization of alkyne **1a** in several solvents



Entry	Solvent	Yield of **2a**+**3a** (%)[a]	**2a**:**3a**[b]
1	Toluene	91	96:4
2	*o*-Xylene	87	96:4
3	Benzene	67	92:8
4	DME	87	91:9
5	1,4-Dioxane	83	93:7
6	THF	47	88:12
7	Et_2O	-	-
8	*i*-PrOH	86	85:15
9	EtOH	55	80:20
10	CH_3CN	50	72:28
11	H_2O	39	89:11
12	1,2-Dichloroethane	59	88:12
13	CH_2Cl_2	18	83:17
14	Hexane	-	-
15	Heptane	3	91:9

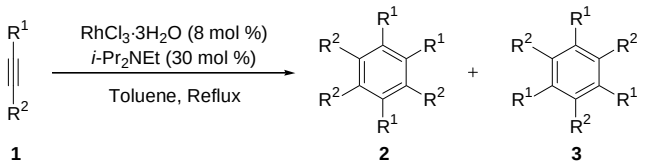
[a] Isolated yield. [b] Determined by ^{1}H NMR.

Next, the $RhCl_3•3H_2O$/*i*-Pr_2NEt catalyst was applied to the cyclotrimerization of various alkynes (Table 5). In the

presence of $RhCl_3$•$3H_2O$ (8 mol %) and *i*-Pr_2NEt (30 mol %), several internal alkynes could successfully undergo the cyclotrimerization to give the corresponding cyclized products (entries 1–11). The cyclotrimerization of alkynes **1a**–**c** bearing phenyl group smoothly proceeded in highly regioselective manner to predominantly afford cycloadducts **2a**–**c**; indeed, the total yields of cycloadducts **2** and **3** were 85–91% and the ratio of **2**:**3** was more than 96:4 (entries 1–3). On the other hand, alkyne **1d** bearing no phenyl group underwent the cyclotrimerization to afford the corresponding adducts, but a slight decline in the regioselectivity was observed (**2d**:**3d** = 76:24) (entry 4). This fact suggested that the regioselectivity of the cyclotrimerization of alkyne was affected by the phenyl group. Notably, in the cyclotrimerization of alkynes **1a**, **1c** and **1d**, the amount of $RhCl_3$•$3H_2O$/*i*-Pr_2NEt could be reduced to 3/9 mol % without an apparent change in the products yields. The cyclotrimerization of symmetrical internal alkynes **1e** and **1f**, gave cycloadducts **2e** and **2f** in respective yields of 96 and 73% (entries 5 and 6). Dimethyl acetylenedicarboxylate (DMAD, **1g**), an active well-used alkyne in cycloaddition, was unsuitable for the reaction (**2g**: 46% yield, entry 7).. As we recently reported, dithienylacetylenes could be utilized in the reaction.[12a] The cyclotrimerization of di(2-thienyl)acetylene and its derivatives (**1h**–**j**) afforded corresponding hexakis(2-thienyl)benzenes (**2h**–**j**) in respective yields of 49, 63, and 50% (entries 8–10). Using di(3-thienyl)acetylene (**1k**), trimerized product **2k** was obtained in 23% yield (entry 11). In a similar manner, terminal alkynes **1l**–**o** were subjected to the Rh/amine-catalyzed trimerization (entries 12–15). The trimerization of phenylacetylene (**1l**) gave cycloadducts **2l** and **3l** in 98% in the ratio of 94:6 (entry 12). The reaction of *p*-tolylacetylene (**1m**) proceeded in a highly selective manner to predominantly afford cyclized products **2m** (total yield 97%) (**2m**:**3m** = >99:<1) (entry 13). The trimerization of 1-octyne (**1n**) afforded cycloadducts **2n** and **3n** in a total yield of 87%, but the ratio of **2n**:**3n** dramatically decreased to 67:33 (entry 14). Upon the cyclotrimerization of ethyl propiolate (**1o**), the yields of the corresponding adduct and the regioselectivity were reduced to 75% and **2o**:**3o** = 74:26 (entry 15). Above all, unsymmetrically substituted acetylene afforded asymmetric adducts **2a**–**d** and **2l**–**o** as the major products in good to excellent yields. The regioselectivity in the $RhCl_3$•$3H_2O$/*i*-Pr_2NEt-catalyzed cyclotrimerization was highly influenced by the aryl substituents of the alkynes; indeed, the cyclotrimerization of alkynes bearing phenyl or tolyl groups proceeded with virtually complete regioselectivities (entries 1–3, 12, and 13).

Table 5

Cyclotrimerization of various alkynes

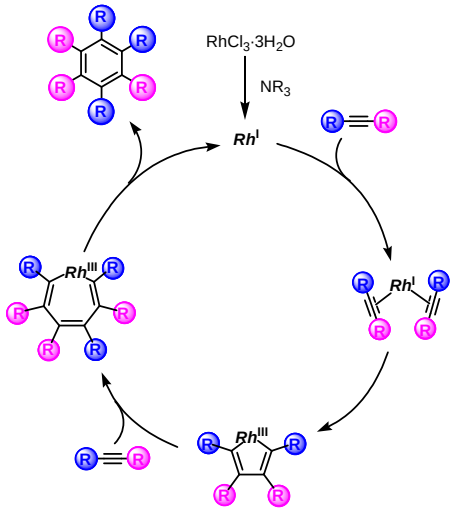


1 **2** **3**

Entry	R^1	R^2		Time (h)	Yield of **2**+**3** (%)[a]	**2**:**3**[b]
1	Ph	CO_2Et	**1a**	24	91 (93)[c]	96:4
2	Ph	CO_2Me	**1b**	24	85	>99:<1
3	Ph	Me	**1c**	24	87 (91)[c]	>99:<1
4	Me	CO_2Et	**1d**	24	95 (90)[c]	76:24
5	Pr	Pr	**1e**	24	96	-
6	Ph	Ph	**1f**	24	73	-
7	CO_2Me	CO_2Me	**1g**	24	46	-
8[d]	2-Thienyl	2-Thienyl	**1h**	24	49	-
9	5-Me-2-thienyl	5-Me-2-thienyl	**1i**	24	63	-
10[d]	5-Ac-2-thienyl	5-Ac-2-thienyl	**1j**	24	50	-
11[d]	3-Thienyl	3-Thienyl	**1k**	24	23	-
12	Ph	H	**1l**	12	98 (94)[c]	94:6
13	*p*-MeC_6H_4	H	**1m**	12	97	>99:<1
14	Hex	H	**1n**	12	87	67:33
15	EtO_2C	H	**1o**	12	75	74:26

[a] Isolated yield. [b] Determined by ^1H NMR. [c] 3 mol % of $RhCl_3$•$3H_2O$ and 9 mol % of *i*-Pr_2NEt were employed. [d] Performed in *i*-PrOH.

The regioselectivity in the $RhCl_3$/amine-catalyzed cyclotrimerization was highly influenced by the substituents of alkynes. In particular, the reaction of alkynes bearing aryl groups proceeded with virtually complete regioselectivities. A plausible mechanism of the reaction is illustrated in Scheme 1. First, $RhCl_3$ would be reduced by *i*-Pr_2NEt to afford a Rh(I) complex. Thus generated electron-rich Rh(I) species might interact with two alkynes by strong π-back donation to form a rhodacyclopentadienyl complex. The insertion of another alkyne to the complex and the subsequent reductive elimination afford the corresponding cyclized product. When alkynes bearing an aryl group were employed, di(α-aryl)rhodacyclopentadienes would be favorable than di(β-aryl) ones. It might be the reason for the regioselective formation of the triarylbenzenes (Table 5, entries 1–3, 12, and 13).



Scheme 1. A plausible mechanism

To obtain further insight into the mechanism, we attempted to capture the *in situ* generated Rh(I) catalyst. To a solution of $RhCl_3$•$3H_2O$ in *i*-PrOH, *i*-Pr_2NEt was added and the mixture was stirred at room temperature for 0.5 h. After the solution was concentrated, the residual black solids were purified by GPC (gel permeation chromatography) to afford the colorless crystals, which were easily deliquescent in air. In the ^1H and ^{13}C NMR spectra of the complex, the peaks of *i*-Pr_2NEt disappeared and new ethyl and isopropyl peaks were observed, suggesting the coordination of *i*-Pr_2NEt to the Rh center (Figures 1 and 2). Though the specific structure of the rhodium complex is not clear at present, the existence of a rhodium complex bearing *i*-Pr_2NEt is strongly indicated.

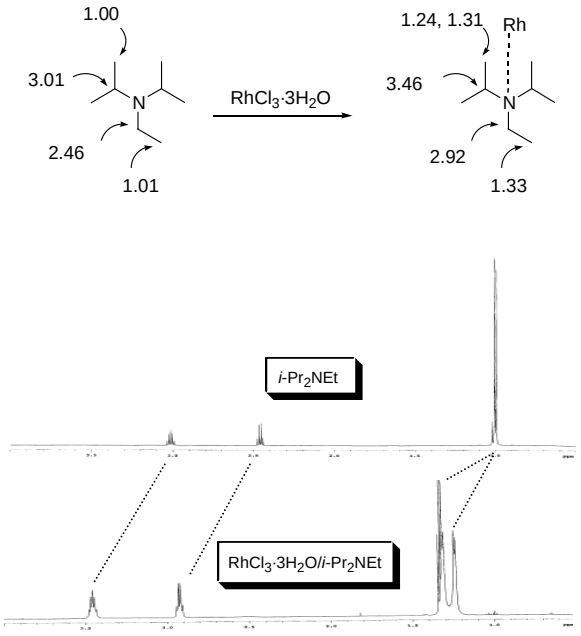
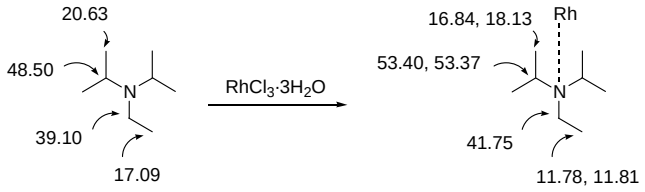


Figure 1. ^1H NMR analysis of *i*-Pr_2NEt and $RhCl_3$•$3H_2O$/*i*-Pr_2NEt complex.



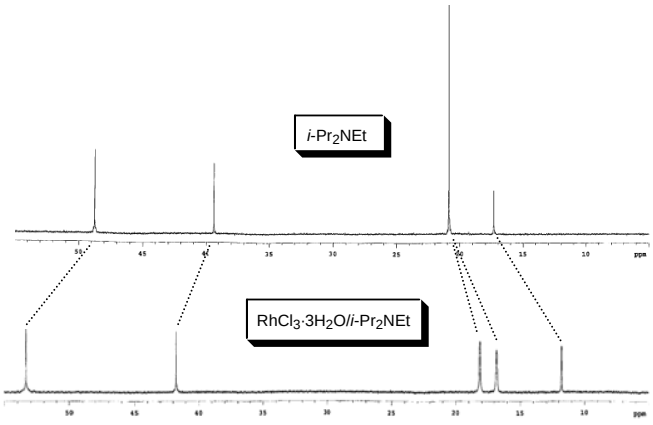
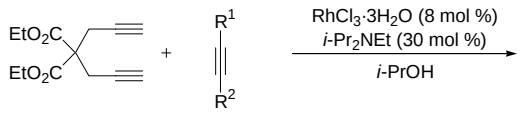


Figure 2. ^{13}C NMR analysis of *i*-Pr_2NEt and $RhCl_3$•$3H_2O$/*i*-Pr_2NEt complex.

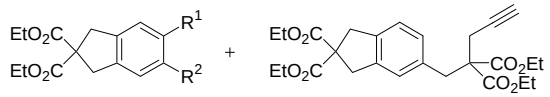
The combination of $RhCl_3$•$3H_2O$ and *i*-Pr_2NEt was successfully used in the [2+2+2] cycloaddition of diyne and various alkynes (Table 6). In the presence of $RhCl_3$•$3H_2O$/*i*-Pr_2NEt, a mixture of diyne **4a** and phenylacetylene (**1l**, 4 equiv) in *i*-PrOH was stirred at 50 °C for 5 h to afford cycloadduct **5al** in 81% yield and 16% of **6a** (entry 1). When the reaction was carried out at reflux, the yields of **5al** and **6a** were almost the same as those in the reaction at 50 °C (entry 2). Next, the $RhCl_3$•$3H_2O$/*i*-Pr_2NEt-catalyzed cyclization of diyne **4a** and 1-octyne (**1n**) was performed at 50 °C for 5 h to afford cycloadduct **5an** in 60% yield (entry 3). When the reaction was carried out at reflux, the yield of **5an** increased to 82% (entry 4). In this case, the reaction proceeded much efficiently at a higher temperature. Internal alkynes could also be utilized in the $RhCl_3$•$3H_2O$/*i*-Pr_2NEt-catalyzed cycloaddition (entries 5–9). Using ethyl phenylpropiolate (**1a**), cyclized product **5aa** was obtained in 39% yield together with 60% of **6a** (entry 5). When the reaction was carried out at reflux, the yield of **5aa** was almost the same as that in the reaction performed at 50 °C, but the yield of **6a** decreased, resulting in the generation of by-products such as polymer (entry 6). The cycloaddition of diyne **4a** and alkyne **1c** at 50 °C or reflux gave the cycloadduct in respective yields of 43 and 48% (entries 7 and 8). When the reaction was carried out using alkyne **1f**, the yield of **5af** was 45% (entry 9). Above all, the $RhCl_3$•$3H_2O$/*i*-Pr_2NEt-catalyzed cyclization of diyne **4a** and terminal alkynes gave the corresponding products in high yields. In the reaction of **4a** and internal alkynes, the yields of dimer **6a** decreased under the refluxing condition, while no significant change was observed in the yields of **5a**, probably because generated **6a** would react with **1** or **4a** to give other products under the refluxing conditions.

Table 6

Cycloaddition of diyne and several alkynes



4a **1** (4 equiv)

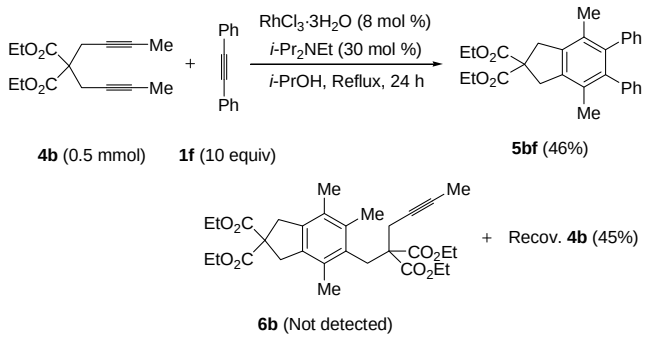


5a **6a**

Entry	R^1	R^2		Temp.	Time (h)		Yield **5a**/**6a** (%)[a]
1	Ph	H	**1l**	50 °C	5	**5al**	81/16
2	Ph	H	**1l**	Reflux	2	**5al**	81/18
3	Hex	H	**1n**	50 °C	5	**5an**	60/27
4	Hex	H	**1n**	Reflux	2	**5an**	82/11
5	Ph	CO_2Et	**1a**	50 °C	5	**5aa**	39/60
6	Ph	CO_2Et	**1a**	Reflux	2	**5aa**	39/17
7	Ph	Me	**1c**	50 °C	5	**5ac**	43/41
8	Ph	Me	**1c**	Reflux	2	**5ac**	48/-
9	Ph	Ph	**1f**	Reflux	2	**5af**	45/-

[a] Isolated yield.

Next, the cycloaddition of diyne **4b** and diphenylacetylene (**1f**) was performed. In the presence of $RhCl_3$•$3H_2O$ (8 mol %) and *i*-Pr_2NEt (30 mol %), to a solution of alkyne **1f** in *i*-PrOH was added dropwise diyne **4b** at reflux, and the mixture was heated to reflux for an additional 24 h to afford **5bf** in 46% yield and 45% of **4b** was recovered (Scheme 2). While the yield of **5bf** was still moderate, the generation of **6b**, the dimer of **4b**, was not observed, and hexa-substituted benzene derivative **5bf** was obtained chemoselectively.



Scheme 2. Cycloaddition of diyne **4b** and diphenylacetylene (**1f**).

3. Conclusion

The [2+2+2] cyclotrimerization of alkynes proceeds with high reactivity when the combination of $RhCl_3$•$3H_2O$/*i*-Pr_2NEt/toluene is used. The reaction can be widely used for various mono- and di-substituted acetylenes and provides tri- or hexa-substituited benzenes regioselectively in high yields. The [2+2+2] cycloaddition of diynes and alkynes has also been developed by using a Rh/amine complex, and it providies benzene derivatives in moderate to high yields.

4. Experimental

4.1. General remarks

^1H and ^{13}C NMR spectra were recorded on Varian INOVA UNITY 600 (^1H 600 MHz, ^{13}C 150 MHz) spectrometers in $CDCl_3$ using TMS or residual chloroform as internal standard. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, double doublet; and tt, triple triplet. Coupling constants are reported in hertz (Hz). IR spectra were recorded on a JASCO FT/IR-4100 spectrophotometer in wave number (cm^{-1}) and only major absorption bands are compiled. Analytic thin layer chromatography (TLC) was performed on Merck, pre-coated plate silica gel 60 F_{254} (0.25 mm thickness). Column chromatography was performed on KANTO CHEMICAL silica gel 60N (40–50 μm). Preparative recycling gel permeation chromatography (GPC) was performed with a JAI LC-9101 instrument equipped with JAIGEL-1H/JAIGEL-2H column using chloroform as an eluent. Elemental analysis was obtained with Perkin-Elmer PE 2400 Series II CHNS/O analyzer. Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. Diynes **4a** and **4b** were prepared according to literature procedures.[14] All reactions were performed in dry solvents under argon atmosphere. Toluene, benzene, xylene, 1,4-dioxane, *i*-PrOH, CH_3CN, dichloroethane, CH_2Cl_2, hexane and heptane were distilled from CaH_2. DME, THF, Et_2O and EtOH were distilled from sodium benzophenone ketyl under argon.

4.2. General procedure for Rh/amine-catalyzed cyclotrimerization of internal alkyne

To a suspension of $RhCl_3$•$3H_2O$ (10 mg, 0.04 mmol) in toluene (3.0 mL) were added *i*-Pr_2NEt (26 μL, 0.15 mmol) and ethyl phenylpropiolate **1a** (87 mg, 0.50 mmol). The mixture was stirred at reflux for 24 h. After being cooled to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/EtOAc 5:1) to afford 1,2,4-triethoxycarbonyl-3,5,6-triphenylbenzene **2a** (79 mg, 91%) as colorless solids.

*4.2.1. 1,2,4-Triethoxycarbonyl-3,5,6-triphenylbenzene (**2a**)*[9d]

Colorless solids; R_f = 0.20 (hexane/EtOAc 5:1); ^1H NMR (600 MHz, $CDCl_3$): δ 0.68 (t, *J* = 7.2 Hz, 3H), 0.87 (t, *J* = 7.2 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H), 3.65 (q, *J* = 7.2 Hz, 2H), 3.94 (q, *J* = 7.2 Hz, 2H), 3.98 (q, *J* = 7.2 Hz, 2H), 7.00–7.04 (m, 4H), 7.11–7.14 (m, 6H), 7.35 (s, 5H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 13.3, 13.41, 13.43, 60.9, 61.50, 61.51, 127.1, 127.3, 127.4, 127.5, 127.9, 128.0, 128.9, 129.8, 129.9, 132.0, 134.1, 137.2, 137.3, 137.4,

137.6, 139.2, 140.7, 167.29, 167.33, 167.7; IR (KBr) 3057, 2981, 2936, 1729, 1232, 1200 cm^{-1}. Anal. Calcd for $C_{33}H_{30}O_6$: C, 75.84; H, 5.79. Found: C, 75.61; H, 5.82.

In a similar manner, the Rh/amine-catalyzed cyclotrimerization of internal alkynes **1b**–**1g** was carried out. The reaction conditions and the results are illustrated in Table 5.

*4.2.2. 1,2,4-Trimethoxycarbonyl-3,5,6-triphenylbenzene (**2b**)*[9d]

Colorless solids; R_f = 0.31 (hexane/EtOAc 1:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.17 (s, 3H), 3.47 (s, 3H), 3.51 (s, 3H), 7.00–7.03 (m, 4H), 7.12–7.15 (m, 6H), 7.32–7.38 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$):□δ 51.7, 52.3, 52.4, 127.2, 127.4, 127.51, 127.52, 128.0, 128.1, 128.5, 129.57, 129.63, 131.7, 134.1, 137.1, 137.20, 137.23, 137.3, 139.2, 140.9, 167.7, 167.9, 168.1; IR (KBr) 3030, 3001, 2951, 1744, 1735, 1244, 1205 cm^{-1}.

*4.2.3. 1,2,4-Trimethyl-3,5,6-triphenylbenzene (**2c**)*[6g]

Colorless solids; R_f = 0.55 (hexane/EtOAc 5:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.72 (s, 3H), 2.04 (s, 3H), 2.05 (s, 3H), 6.96–7.14 (m, 10H), 7.25 (dd, *J* = 7.8, 1.2 Hz, 2H), 7.35 (tt, *J* = 7.8, 1.2 Hz, 1H), 7.45 (tm, *J* = 7.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 18.1, 18.3, 19.4, 125.6, 125.7, 126.5, 127.28, 127.31, 128.4, 129.4, 130.286, 130.294, 131.3, 131.9, 133.9, 139.2, 140.6, 141.4, 141.58, 141.61, 142.4; IR (KBr) 3055, 2956, 2918, 2849 cm^{-1}.

*4.2.4. 1,2,4-Triethoxycarbonyl-3,5,6-trimethylbenzene (**2d**)*[2e]

Colorless liquid; R_f = 0.13 (hexane/EtOAc 5:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ□1.35 (t, *J* = 7.2 Hz, 3H), 1.36 (t, *J* = 7.2 Hz, 3H), 1.38 (t, *J* = 7.2 Hz, 3H), 2.22 (s, 3H), 2.26 (s, 3H), 2.30 (s, 3H), 4.32 (q, *J* = 7.2 Hz, 2H), 4.33 (q, *J* = 7.2 Hz, 2H), 4.40 (q, *J* = 7.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ14.0, 14.2, 16.5, 17.0, 17.3, 61.37, 61.46, 61.49, 129.9, 130.3, 132.6, 133.7, 135.8, 137.5, 167.8, 168.5, 169.4; IR (neat) 2982, 2938, 2906, 1731, 1576 cm^{-1}. Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 64.02; H, 7.13.

*4.2.5. 1,3,5-Triethoxycarbonyl-2,4,6-trimethylbenzene (**3d**)*[2e]

Colorless liquid; R_f = 0.20 (hexane/EtOAc 5:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ□1.37 (t, *J* = 7.2 Hz, 9H), 2.23 (s, 9H), 4.38 (q, *J* = 7.2 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 14.2, 17.1, 61.3, 132.1, 133.5, 169.0; IR (neat) 2981, 2937, 1728, 1581, 1226 cm^{-1}. Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 64.34; H, 7.29.

*4.2.6. Hexapropylbenzene (**2e**)*[4e]

Colorless solids; R_f = 0.80 (hexane/EtOAc 5:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.04 (t, *J* = 7.2 Hz, 18H), 1.49–1.57 (m, 12H), 2.46–2.48 (m, 12H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 15.3, 24.8, 32.2, 136.7; IR (KBr) 2952, 2928, 2890, 2869 cm^{-1}. Anal. Calcd for $C_{24}H_{42}$: C, 87.19; H, 12.81. Found: C, 87.21; H, 13.14.

*4.2.7. Hexaphenylbenzene (**2f**)*[6g]

Colorless solids; R_f = 0.50 (hexane/EtOAc 5:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.83–6.86 (m, 30H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 125.2, 126.5, 131.4, 140.3, 140.6; IR (KBr) 3056, 3024, 2925 cm^{-1}.

*4.2.8. Hexamethoxycarbonylbenzene (**2g**)*

Colorless solids; R_f = 0.31 (hexane/EtOAc 1:1), ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.88 (s, 18H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 53.5, 133.9, 165.1; IR (KBr) 3009, 2958, 1739, 1445 cm^{-1}; Anal. Calcd for $C_{18}H_{18}O_6$: C, 50.71; H, 4.26. Found: C, 50.77; H, 3.99.

4.3. General procedure for Rh/amine-catalyzed cyclotrimerization of di(thienyl)acetylene

To a solution of $RhCl_3 \cdot 3H_2O$ (11 mg, 0.04 mmol) in *i*-PrOH (3.0 mL) were added *i*-Pr_2NEt (26 μL, 0.15 mmol) and di(2-thienyl)acetylene **1h** (96 mg, 0.50 mmol). The mixture was stirred at reflux for 24 h. After being cooled to room temperature, the reaction mixture was filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/toluene 5:1) to afford hexa(2-thienyl)benzene **2h** (47 mg, 49%) as yellow solids.

*4.3.1. Hexa(2-thienyl)benzene (**2h**)*

Yellow solids; R_f = 0.27 (hexane/toluene 5:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.59 (dd, *J* = 3.6, 1.2 Hz, 6H), 6.68 (dd, *J* = 5.4, 3.6 Hz, 6H), 7.08 (dd, *J* = 5.4, 1.2 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 125.8, 126.2, 129.1, 137.0, 140.7; IR (KBr) 3068, 2923, 2360, 1647, 1381, 694 cm^{-1}; Anal. Calcd for $C_{30}H_{18}S_6$: C, 63.12; H, 3.18. Found: C, 63.08; H, 3.36.

In a similar manner, the Rh/amine-catalyzed cyclotrimerization of di(thienyl)acetylene derivatives **1i**–**1k** was carried out. The reaction conditions and the results are illustrated in Table 5.

*4.3.2. Hexakis(5-methyl-2-thienyl)benzene (**2i**)*

Yellow solids; R_f = 0.23 (hexane/toluene 5:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.33 (s, 12H), 2.30 (s, 18H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 15.2, 123.9, 128.7, 137.0, 138.8, 140.2; IR (KBr) 3068, 2912, 2855, 2357, 1747, 1442, 1219, 800 cm^{-1}; Anal. Calcd for $C_{36}H_{30}S_6$: C, 66.01; H, 4.62. Found: C, 66.09; H, 4.53.

*4.3.3. Hexakis(5-acetyl-2-thienyl)benzene (**2j**)*

Colorless solids; R_f = 0.07 (hexane/EtOAc 3:1), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.27 (d, *J* = 3.6 Hz, 6H), 6.67 (d, *J* = 3.6 Hz, 6H), 2.43 (s, 18H); ^{13}C NMR (150 MHz, $CDCl_3$) δ

26.7, 130.9, 131.8, 136.5, 145.8, 146.7, 190.7; IR (KBr) 3080, 1658, 1471, 1381, 1274 cm^{-1}.

*4.3.4. Hexa(3-thienyl)benzene (**2k**)*

Brown solids; R_f = 0.27 (hexane/EtOAc 3:1), ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.91 (dd, *J* = 4.8, 3.0 Hz, 6H), 6.58 (dd, *J* = 3.0, 1.5 Hz, 6H), 6.50 (dd, *J* = 4.8, 3.6 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 123.3, 124.1, 129.7, 136.5, 140.3; IR (KBr) 3068, 2923, 2360, 1647, 1381, 1223, 694 cm^{-1}; Anal. Calcd for $C_{30}H_{18}S_6$: C, 63.12; H, 3.18. Found: C, 63.08; H, 3.36.

4.4. General procedure for Rh/amine-catalyzed cyclotrimerization of terminal alkyne

To a suspension of $RhCl_3$•$3H_2O$ (11 mg, 0.04 mmol) in toluene (3.0 mL) were added *i*-Pr_2NEt (26 μL, 0.15 mmol) and phenylacetylene **1l** (55 mg, 0.50 mmol). The mixture was stirred at reflux for 12 h. After being cooled to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/EtOAc 5:1) to afford 1,2,4-triphenylbenzene **2l** (54 mg, 98%) as colorless solids.

*4.4.1. 1,2,4-Triphenylbenzene (**2l**)[7a,15]*

Colorless solids; R_f = 0.57 (hexane/EtOAc 5:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.17–7.24 (m, 10H), 7.37 (tt, *J* = 7.8, 1.2 Hz, 1H), 7.45–7.48 (m, 2H), 7.51 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.65–7.69 (m, 4H): ^{13}C NMR (150 MHz, $CDCl_3$): δ 126.1, 126.5, 126.6, 127.1, 127.4, 127.89, 127.92, 128.8, 129.4, 129.87, 129.90, 131.1, 139.5, 140.4, 140.6, 141.0, 141.1, 141.5; IR (KBr) 3075, 3056, 3027 cm^{-1}.

In a similar manner, the Rh/amine-catalyzed cyclotrimerization of terminal alkynes **1m**–**1o** was conducted. The reaction conditions and the results are illustrated in Table 5.

*4.4.2. 1,2,4-Tris(4-methylphenyl)benzene (**2m**)[3g,4e]*

Colorless solids; R_f = 0.60 (hexane/EtOAc 5:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.32 (s, 3H), 2.33 (s, 3H), 2.40 (s, 3H), 7.03–7.10 (m, 8H), 7.26 (dd, *J* = 7.8, 0.6 Hz, 2H), 7.46 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.56–7.62 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.11, 21.13, 125.7, 126.9, 128.6, 128.7, 129.2, 129.5, 129.68, 129.71, 131.1, 136.0, 136.1, 137.1, 137.8, 138.3, 138.7, 139.1, 140.0, 140.8; IR (KBr) 3025, 2917, 2863 cm^{-1}. Anal. Calcd for $C_{27}H_{24}$: C, 93.06; H, 6.94. Found: C, 92.67; H, 7.33.

*4.4.3. 1,2,4-Trihexylbenzene (**2n**)[4e]*

Colorless liquid; R_f = 0.77 (hexane/EtOAc 5:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.87–0.91 (m, 9H), 1.28–1.39 (m, 18H), 1.54–1.59 (m, 6H), 2.52–2.58 (m, 6H), 6.92 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.95 (d, *J* = 1.8 Hz, 1H), 7.04 (d, *J* = 7.8 Hz, 1H).

*4.4.4. 1,2,4-Triethoxycarbonylbenzene (**2o**)[3d]*

Yellow liquid; R_f = 0.23 (hexane/EtOAc 5:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.38 (t, *J* = 7.2 Hz, 3H), 1.39 (t, *J* = 7.2 Hz, 3H), 1.41 (t, *J* = 7.2 Hz, 3H), 4.39 (q, *J* = 7.2 Hz, 4H), 4.41 (q, *J* = 7.2 Hz, 2H), 7.76 (dd, *J* = 8.4, 0.6 Hz, 1H), 8.19 (dd, *J* = 8.4, 1.2 Hz, 1H), 8.40 (dd, *J* = 1.2, 0.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 14.0, 14.1, 14.2, 61.7, 61.9, 62.0, 128.8, 130.1, 132.00, 132.04, 132.7, 136.2, 165.0, 166.6, 167.2; IR (neat) 2983, 2938, 1727, 1244 cm^{-1}. Anal. Calcd for $C_{15}H_{18}O_6$: C, 61.22; H, 6.16. Found: C, 61.14; H, 6.60.

*4.4.5. 1,3,5-Triethoxycarbonylbenzene (**3o**)[16]*

Colorless solids; R_f = 0.23 (hexane/EtOAc 5:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.43 (t, *J* = 7.2 Hz, 9H), 4.44 (q, *J* = 7.2 Hz, 6H), 8.85 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 14.3, 61.7, 131.4, 134.4, 165.1; IR (KBr) 2943, 2907, 2877, 1724, 1240 cm^{-1}. Anal. Calcd for $C_{15}H_{18}O_6$: C, 61.22; H, 6.16. Found: C, 61.46; H, 6.28.

*4.5. Synthesis of $RhCl_3$•$3H_2O$/*i*-Pr_2NEt complex*

To a solution of $RhCl_3$•$3H_2O$ (26 mg, 0.1 mmol) in *i*-PrOH (6 mL) was added *i*-Pr_2NEt (51 μL, 0.3 mmol). The mixture was stirred at room temperature (or reflux) for 0.5 h, and was concentrated under reduced pressure. The residue was purified by gel permeation chromatography. Then the solid was purified by recyclization, and colorless crystals were obtained.

*4.6. General Procedure for Cyclization of Diyne **4a** and Alkyne **1***

To a solution of $RhCl_3$•$3H_2O$ (11 mg, 0.04 mmol) and *i*-Pr_2NEt (26 μL, 0.15 mmol) in *i*-PrOH (2.0 mL) were added phenylacetylene **1l** (217 mg, 2.0 mmol) and diyne **4a** (116 mg, 0.49 mmol) in *i*-PrOH (3.0 mL). The mixture was stirred at reflux for 2 h. After being cooled to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/EtOAc 5:1) to afford diethyl 5-phenyl-1*H*-indene-2,2(3*H*)-dicarboxylate **5al** (138 mg, 81%) as yellow liquid.

*4.6.1. Diethyl 5-Phenyl-1H-indene-2,2(3H)-dicarboxylate (**5al**)[6e]*

Yellow liquid; R_f = 0.37 (hexane/EtOAc 5:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.25–1.28 (m, 6H), 3.63 (s, 2H), 3.66 (s, 2H), 4.26 (q, *J* = 7.2 Hz, 4H), 7.26–7.27 (m, 1H), 7.32–7.34 (m, 1H), 7.39–7.43 (m, 4H), 7.55–7.56 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 14.0, 40.2, 40.4, 60.5, 61.7, 123.0, 124.4, 126.1, 127.0, 127.1, 128.6, 139.1, 140.3, 140.7, 141.3, 171.6; IR (neat) 3031, 2980, 2936, 1733 cm^{-1}. Anal. Calcd for $C_{21}H_{22}O_4$: C, 74.54; H, 6.56. Found: C, 74.53; H, 6.74.

In a similar manner, the Rh/amine-catalyzed cyclotrimerization of diyne **4a** and alkynes **1a, 1c, 1f,** and **1n** was carried out. The reaction conditions and the results are illustrated in Table 6.

*4.6.2. Diethyl 5-Hexyl-1H-indene-2,2(3H)-dicarboxylate (**5an**)*[2e]

Orange liquid; R_f = 0.47 (hexane/EtOAc 5:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.87–0.89 (m, 3H), 1.24–1.33 (m, 12H), 1.54–1.60 (m, 2H), 2.54 (t, *J* = 7.2 Hz, 2H), 3.55 (s, 2H), 3.56 (s, 2H), 4.20 (q, *J* = 7.2 Hz, 4H), 6.97 (d, *J* = 7.2 Hz, 1H), 7.01 (s, 1H), 7.08 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 14.0, 14.1, 22.6, 29.0, 31.69, 31.72, 35.8, 40.1, 40.4, 60.5, 61.6, 123.8, 124.1, 127.1, 137.1, 140.0, 141.8, 171.8; IR (neat) 2957, 2928, 2856, 1735 cm^{-1}. Anal. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.79; H, 8.84.

*4.6.3. Diethyl 5-Ethoxycarbonyl 6-Phenyl-1H-indene-2,2(3H)-dicarboxylate (**5aa**)*

Colorless solids; R_f = 0.26 (hexane/EtOAc 4:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.96 (t, *J* = 7.2 Hz, 3H), 1.27 (t, *J* = 7.2 Hz, 6H), 3.63 (s, 2H), 3.65 (s, 2H), 4.04 (q, *J* = 7.2 Hz, 2H), 4.22 (q, *J* = 7.2 Hz, 2H), 7.19 (d, *J* = 0.6 Hz, 1H), 7.26–7.28 (m, 2H), 7.30–7.37 (m, 2H), 7.66 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 13.6, 14.0, 40.0, 40.4, 60.4, 60.8, 61.8, 125.5, 126.4, 126.9, 127.9, 128.3, 130.2, 139.2, 141.66, 141.74, 143.7, 168.8, 171.3; IR (KBr) 3059, 3024, 2980, 2935, 2905, 1732 cm^{-1}. Anal. Calcd for $C_{24}H_{26}O_6$: C, 70.23; H, 6.38. Found: C, 70.15; H, 6.44.

*4.6.4. Diethyl 5-Methyl 6-Phenyl-1H-indene-2,2(3H)-dicarboxylate (**5ac**)*

Yellow liquid; R_f = 0.40 (hexane/EtOAc 5:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.27 (t, *J* = 7.2 Hz, 6H), 2.21 (s, 3H), 3.59 (s, 2H), 3.60 (s, 2H), 4.22 (q, *J* = 7.2 Hz, 4H), 7.05 (s, 1H), 7.10 (s, 1H), 7.28–7.33 (m, 3H), 7.37–7.40 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 14.0, 20.4, 40.2, 40.3, 60.5, 61.7, 125.5, 126.6, 128.0, 129.2, 134.1, 137.5, 139.1, 140.8, 142.1, 171.7; IR (neat) 3057, 2980, 2935, 1733, 1244 cm^{-1}. Anal. Calcd for $C_{22}H_{24}O_4$: C, 74.98; H, 6.86. Found: C, 74.93; H, 6.99.

*4.6.5. Diethyl 5,6-Diphenyl-1H-indene-2,2(3H)-dicarboxylate (**5af**)*

Colorless solids; R_f = 0.39 (hexane/EtOAc 4:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.281 (t, *J* = 7.2 Hz, 3H), 1.282 (t, *J* = 7.2 Hz, 3H), 3.68 (s, 4H), 4.240 (q, *J* = 7.2 Hz, 2H), 4.241 (q, *J* = 7.2 Hz, 2H), 7.09–7.11 (m, 4H), 7.15–7.20 (m, 6H), 7.25 (d, *J* = 0.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 14.0, 40.3, 60.5, 61.8, 126.3, 127.8, 129.9, 139.4, 139.6, 141.6, 171.7; IR (KBr) 3057, 2985, 2903, 1732, 1708 cm^{-1}.

*4.7. General Procedure for Cyclization of Diyne **4b** and Alkyne **1f***

To a solution of $RhCl_3$•$3H_2O$ (11 mg, 0.04 mmol) and *i*-Pr_2NEt (26 μL, 0.15 mmol) in *i*-PrOH (2.0 mL) were added diphenylacetylene **1f** (900 mg, 5.0 mmol) and diyne **4b** (132 mg, 0.50 mmol) in *i*-PrOH (3.0 mL). The mixture was stirred at reflux for 24 h. After being cooled to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/EtOAc 5:1) to afford diethyl 4,7-dimethyl-5,6-diphenyl-1*H*-indene-2,2(3*H*)-dicarboxylate **5bf** (102 mg, 46%) and 45% of **4b** was recovered.

*Diethyl 4,7-Dimethyl-5,6-diphenyl-1H-indene-2,2(3H)-dicarboxylate (**5bf**)*

Red liquid; R_f = 0.50 (hexane/EtOAc 5:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.32 (t, *J* = 7.2 Hz, 6H), 2.00 (s, 6H), 3.69 (s, 4H), 4.28 (q, *J* = 7.2 Hz, 4H), 6.92 (d, *J* = 7.2 Hz, 4H), 7.04–7.06 (m, 2H), 7.10–7.12 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 13.7, 19.2, 30.7, 64.4, 118.2, 128.0, 128.8, 130.2, 134.4, 144.5, 167.1; IR (neat) 3056, 3021, 2981, 2935, 1733, 1242 cm^{-1}.

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Supplementary material

Supplementary material and representative spectra associated with this article can be found in the online version, at doi:

Reference and notes

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