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Rhenium- and Manganese-Catalyzed Synthesis of Aromatic Compounds from 1,3-Dicarbonyl Compounds and Alkynes

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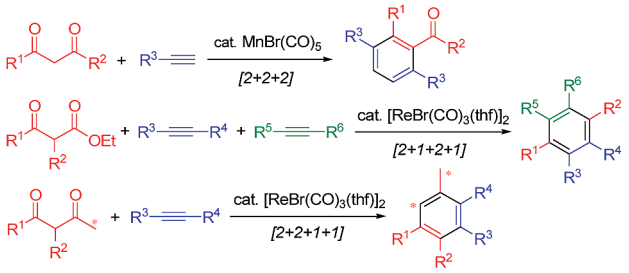

We have succeeded in the development of three approaches to the synthesis of aromatic compounds from 1,3-dicarbonyl compounds and alkynes. The first approach is a manganese-catalyzed [2+2+2] cycloaddition between 1,3-dicarbonyl compounds, which have no substituents at the active methylene moiety, and terminal alkynes. This reaction proceeds with high regioselectivity when aryl acetylenes are employed as the alkyne component. The second approach is a rhenium- or manganese-catalyzed formal [2+1+2+1] cycloaddition between β-keto esters and two kinds of alkynes. In this reaction, the aromatic compounds are obtained by the following reaction sequence: (1) insertion of the first alkyne into a carbon−carbon single bond of a β-keto ester, (2) formation of 2-pyranones via intramolecular cyclization with the elimination of ethanol, and (3) Diels−Alder reaction between the formed 2-pyranone and the second alkyne. This reaction provides multisubstituted aromatic compounds in a regioselective manner. The third approach is a rhenium-catalyzed formal [2+2+1+1] cycloaddition reaction from two 1,3-diketones and one alkyne. In this reaction, the aromatic skeleton is constructed from three carbons of the first 1,3-diketone, two carbons of the alkyne, and one carbon of the second 1,3-diketone.

Introduction

Aromatic compounds play an important role in organic chemistry, serving as functional materials and bioactive compounds. This has led to many reports on the synthesis of aromatic compounds including transition metal-catalyzed [2+2+2] cycloaddition reactions of alkynes, which are popular and atom-economical.[1] However, due to the low pair- and regioselectivity of the [2+2+2] cycloaddition, it does not lend itself to the easy introduction of different substituents on the aromatic skeleton from two or three kinds of alkynes. Recently, to overcome this limitation, research has focused on new approaches to the synthesis of multisubstituted aromatic compounds.[2] During our investigations of rhenium- and manganese-catalyzed reactions,[3,4] we found that

(1) (a) Grotjahn, D. B. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, UK, 1995; Vol. 12, pp 741−770. (b) Bonnemann, H.; Brijoux, W. In *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, Germany, 2004; Vol. 1, pp 171−197.

(2) (a) Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 539. (b) Saito, S.; Yamamoto, Y. *Chem. Rev.* **2000**, *100*, 2901. (c) Mori, N.; Ikeda, S.; Odashima, K. *Chem. Commun.* **2001**, 181.

(3) For rhenium-catalyzed reactions, see: (a) Kuninobu, Y.; Kawata, A.; Takai, K. *J. Am. Chem. Soc.* **2005**, *127*, 13498. (b) Yudha, S. S.; Kuninobu, Y.; Takai, K. *Org. Lett.* **2007**, *9*, 5609. (c) Kuninobu, Y.; Nishina, Y.; Matsuki, T.; Takai, K. *J. Am. Chem. Soc.* **2008**, *130*, 14062. (d) Yudha, S. S.; Kuninobu, Y.; Takai, K. *Angew. Chem., Int. Ed.* **2008**, *47*, 9318.

(4) For manganese-catalyzed reactions, see: (a) Kuninobu, Y.; Nishina, Y.; Takeuchi, T.; Takai, K. *Angew. Chem., Int. Ed.* **2007**, *46*, 6518. (b) Kuninobu, Y.; Kikuchi, K.; Takai, K. *Chem. Lett.* **2008**, *37*, 740.

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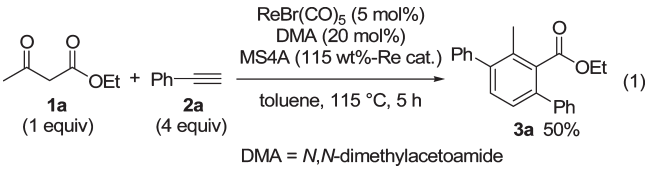
substituted aromatic compounds could be obtained regioselectively from 1,3-dicarbonyl compounds and two alkynes by changing the catalysts, additives, and/or reaction conditions. In this paper, we report the scope and limitations of the reactions and their reaction mechanisms.

Results and Discussion

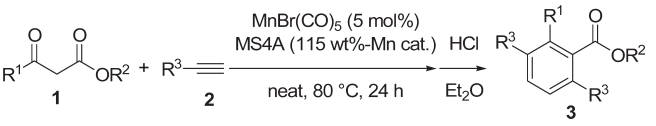
Manganese-Catalyzed Synthesis of Tetra- and Trisubstituted Aromatic Compounds via [2+2+2] Cycloaddition. In 2005, we reported on the addition of 1,3-dicarbonyl compounds to terminal alkynes, where alkenylation of the active methylene moiety of 1,3-dicarbonyl compounds occurred.[5] During the investigation of additives, we found a quite different reaction accidentally. By adding a catalytic amount of *N*,*N*-dimethylacetoamide (DMA), a tetrasubstituted aromatic compound **3a** was formed in 50% yield from a β-keto ester **1a** and 2 equiv of phenylacetylene (**2a**) (eq 1).[6]



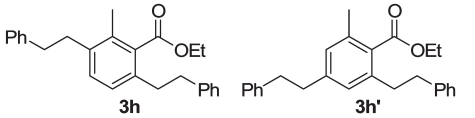
The yield of the tetrasubstituted aromatic compound **3a** was improved by using a manganese complex, $MnBr(CO)_5$, as a catalyst (Table 1, entry 1).[6,7] In this system, DMA was not necessary to promote the reaction. Tetrasubstituted aromatic compounds could be synthesized regioselectively by changing the substituents on the β-keto esters (Table 1, entries 2 and 3). This reaction is suitable for the synthesis of *p*-terphenyl derivatives (Table 1, entries 4−7). Aryl acetylenes with either an electron-donating group, **2b** and **2c**, or a bromo atom, **2d**, provided the corresponding terphenyls **3d**−**f** in good yields (Table 1, entries 4−6). In the case of **2d**, side reactions did not occur at the carbon−bromine bond (entry 6). 1,4-Dinaphthalenylbenzene **3g** was also produced with alkyne **2e** (Table 1, entry 7). Although the aryl acetylenes **2a**−**e** afforded only single products, a mixture of two isomers **3h** and **3h′** was generated when alkylacetylene **2f** was used (Table 1, entry 8). This reaction did not proceed with β-keto esters with a substituent at the active methylene moiety.[8] Also, the reaction did not occur with internal alkynes.

This reaction also proceeded with 1,3-diketones as substrates; however, the products were different (eq 2). Treatment of 1,3-diketone **4a** with phenylacetylene (**2a**) in the presence of a manganese catalyst, $MnBr(CO)_5$, and molecular sieves in toluene produced tetrasubstituted acetophenone derivative **5** in 69% yield. In this reaction, alkenylated product **7** was formed in 7% yield as a side product. Interestingly, deacylated aromatic compound **6** was also obtained in 5% yield. To improve the yield of the trisubstituted aromatic compound **6**, we investigated the reaction conditions. As a result, aromatic compound **6** was afforded in 66% yield when the reaction was carried out at 80 °C in a mixture of toluene and water (1:1). By using a catalytic amount of $Sc(OTf)_3$, the yield of **6** increased slightly.

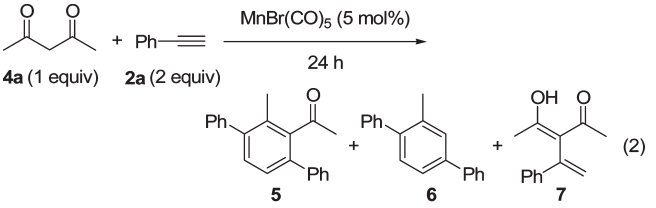
TABLE 1. Reactions between β-Keto Esters 1 and Alkynes 2[a]



entry	R^1	R^2		R^3			% yield
1	Me	Et	**1a**	Ph	**2a**	**3a**	85
2	Me	Me	**1b**		**2a**	**3b**	65
3	Ph	Et	**1c**		**2a**	**3c**	88
4		**1c**		MeO	**2b**	**3d**	77
5		**1c**		OMe	**2c**	**3e**	74
6		**1c**		Br	**2d**	**3f**	86
7		**1c**		MeO	**2e**	**3g**	71
8		**1c**		Ph	**2f**	**3h** + **3h'**	88 [2.7:1][b]

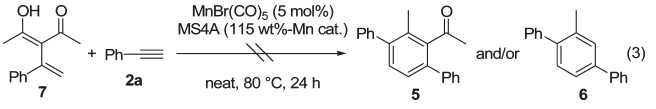


[a] **1** (1 equiv), **2** (2.5 equiv). [b] The ratio between **3h** and **3h′**.



temp [°C]	additive	solvent	% yield[a] 5	6	7
50	MS4A (115 wt%-Mn)	toluene	69 (71)	5 (7)	7 (10)
80	none	toluene / H_2O (1:1)	20 (24)	66 (68)	- (trace)
80	$Sc(OTf)_3$ (5 mol%)	toluene / H_2O (1:1)	16 (20)	68 (70)	4 (6)

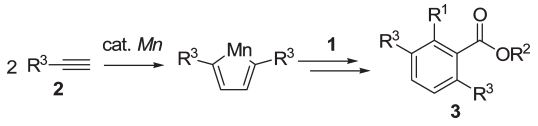
To confirm if the tetra- and trisubstituted aromatic compounds, **5** and **6**, are formed from alkenylated product **7** and phenylacetylene (**2a**), the reaction shown in eq 3 was carried out. However, neither of the aromatic compounds was produced showing that this was not the case.



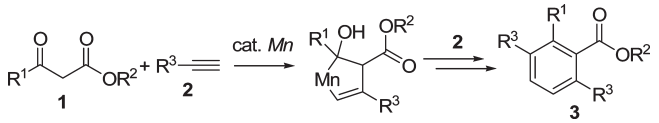
To explain the formation of the tetrasubstituted aromatic compounds **3** and their regiochemistry, there are three

(5) Kuninobu, Y.; Kawata, A.; Takai, K. *Org. Lett.* **2005**, *7*, 4823.
(6) Kuninobu, Y.; Nishi, M.; Yudha, S. S.; Takai, K. *Org. Lett.* **2008**, *10*, 3009.
(7) Another group also reported on the similar manganese-catalyzed reaction. See: Tsuji, H.; Yamagata, K.-i.; Fujimoto, T.; Nakamura, E. *J. Am. Chem. Soc.* **2008**, *130*, 7792.
(8) When β-keto esters with a substituent at the active methylene moiety were used, insertion of alkynes into a carbon−carbon bond of β-keto esters occurred, and successive intramolecular cyclization gave 2-pyranones. See: Kuninobu, Y.; Kawata, A.; Nishi, M.; Takata, H.; Takai, K. *Chem. Commun.* **2008**, 6360.

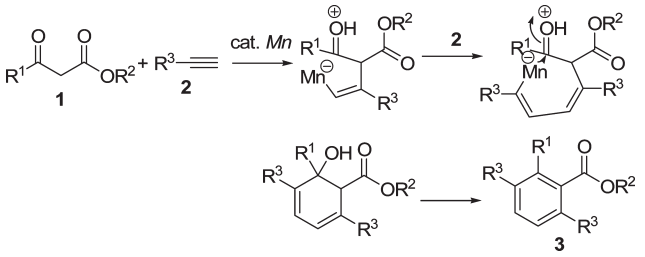
SCHEME 1. Formation of Tetrasubstituted Aromatic Compounds 3 via a Manganacyclopentadiene Intermediate



SCHEME 2. Formation of Tetrasubstituted Aromatic Compounds 3 via an Alkenyl-Manganese Intermediate

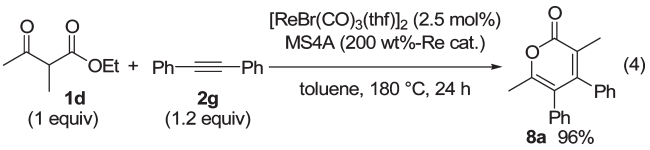


SCHEME 3. Formation of Tetrasubstituted Aromatic Compounds 3 via an Alkenyl-Manganese Intermediate



possible reaction pathways (Schemes 1−3). The first is that the reaction proceeds via the formation of a manganacyclopentadiene intermediate, which suggests that two substituents are located at the 2- and 5-positions due to the steric factor (Scheme 1). The second possibility is that the reaction proceeds via the formation of a metalacyclopentene intermediate, which is produced by a reaction between a 1, 3-dicarbonyl compound and an alkyne (Scheme 2).[9] The third possibility is the formation of an alkenyl-manganese intermediate via the stepwise insertion of two alkynes in the opposite orientation to each other (Scheme 3). Very recently, Nakamura, Tsuji, and co-workers reported on the mechanistic study of the [2+2+2] cycloaddition.[10] In the paper, they concluded that the reaction proceeds via the route shown in Scheme 3.

Rhenium-Catalyzed Synthesis of Penta- and Hexasubsitituted Aromatic Compounds via Carbon−Carbon Bond Cleavage of *β*-Keto Esters. When *β*-keto esters with a substituent at the active methylene moiety were employed, the structure of the products was changed dramatically, as can be seen by comparing the products obtained in eq 1 with those in eq 4. Treatment of ethyl 2-methyl-3-oxobutanoate (**1d**) with diphenylacetylene (**2g**) in the presence of a catalytic amount of a rhenium complex, $[ReBr(CO)_3(thf)]_2$, and molecular sieves in toluene at 180 °C for 24 h, resulted in the insertion of **2g** into a carbon−carbon single bond of **1d** and successive intramolecular nucleophilic addition via the elimination of ethanol, to obtain the 2-pyranone derivative **8a** in 96% yield (eq 4).[11,12]



2-Pyranone derivatives are good precursors to synthesize aromatic compounds via the Diels−Alder reaction.[13] Thus, the reactions in eq 4 could be applied to the synthesis of multisubstituted aromatic compounds (Table 2). By the reaction of *β*-keto ester **1d** with diphenylacetylene (**2g**) in the presence of $[ReBr(CO)_3(thf)]_2$ as a catalyst, followed by treatment with a catalytic amount of tetrabutylammonium fluoride (TBAF) and heating with alkyne **9a**, an aromatization reaction proceeded and hexasubstituted benzene derivative **10a** was obtained in 83% yield (entry 1). A *β*-keto ester bearing a phenyl group at the *β*-position, **1e**, and without a substituent at the active methylene moiety, **1a**, provided multisubstituted aromatic compounds, **10b** and **10c**, in 64% and 84% yields, respectively (entries 2 and 3). When an internal alkyne was employed, the structure of the products changed dramatically, as can be seen by comparing the products obtained in eq 1 with those in Table 2, entry 3. 1-Phenyl-1-propyne (**2h**) and terminal acetylenes, such as phenylacetylene (**2a**) and 1-dodecyne (**2i**), also afforded polysubstituted aromatic compounds in good to excellent yields (entries 4−8).[14] Interestingly, in the case of terminal acetylenes, **2a** and **2i**, the addition of TBAF lowered the reaction temperature dramatically, and 2-pyranone derivatives **8** were formed under milder conditions (entries 6 and 8).[8] Two regioisomers of hexasubstituted aromatic compounds, **10g** and **10h**, could be synthesized selectively by exchanging two substituents of the *β*-keto esters, **1f** and **1g** (entries 9 and 10). In this reaction, the regioselective insertion of alkynes into a carbon−carbon bond is important to generate **10g** and **10h**, selectively. Ethyl propiolate (**9b**) also afforded pentasubstituted aromatic compounds, **10i** and a mixture of **10j** + **10k**, in 86% and 77% (**10j**:**10k** = 39:61) yields, respectively (entries 11 and 12).

The regioselective synthesis of a multisubstituted aromatic compound could also be achieved with use of a manganese complex, $MnBr(CO)_5$, as a catalyst; however, the yield of the multisubstituted aromatic compound was lower than that of the rhenium-catalyzed transformation. For example,

(9) The intermediate shown in Scheme 2 is thought to be a manganese- and rhenium-catalyzed ring expansion and carbon-chain extension reaction. See: Kuninobu, Y.; Kawata, A.; Takai, K. *J. Am. Chem. Soc.* **2006**, *128*, 11368. See also ref 8.

(10) Nakamura's group reported on the mechanistic investigations. In the paper, they claimed that the reaction must proceed via the formation of alkenyl-magnesium intermediate (Scheme 3). See: Yoshikai, N.; Zhang, S.; Yamagata, K.-i.; Tsuji, H.; Nakamura, E. *J. Am. Chem. Soc.* **2009**, *131*, 4099.

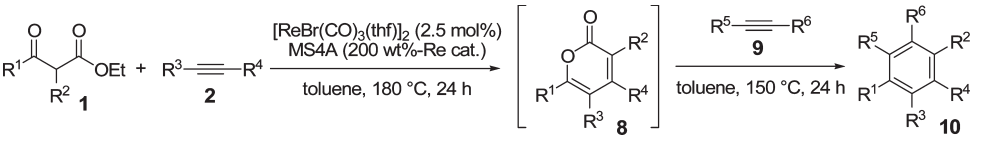
(11) Kuninobu, Y.; Takata, H.; Kawata, A.; Takai, K. *Org. Lett.* **2008**, *10*, 3133.

(12) For some representative examples of 2-pyranone synthesis, see: (a) Cho, S. H.; Liebeskind, L. S. *J. Org. Chem.* **1987**, *52*, 2631. (b) Tsuda, T.; Morikawa, S.; Sumiya, R.; Saegusa, T. *J. Org. Chem.* **1988**, *53*, 3140. (c) Larock, R. C.; Han, X.; Doty, M. J. *Tetrahedron Lett.* **1998**, *39*, 5713. (d) Fukuyama, T.; Higashibeppu, Y.; Yamaura, R.; Ryu, I. *Org. Lett.* **2007**, *9*, 587.

(13) For the formation of aromatic compounds from 2-pyranones and acetylenes, see: (a) Tam, T. F.; Coles, P. *Synthesis* **1988**, 383. (b) Afarinkia, K.; Vinader, V.; Nelson, T. D.; Posner, G. H. *Tetrahedron* **1992**, *48*, 9111.

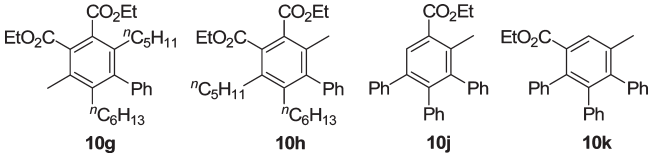
(14) Diels−Alder reactions between 2-pyranone **8b** and alkyne **9a** were investigated in the presence or absence of a rhenium catalyst, $[ReBr(CO)_3(thf)]_2$, and MS4A to clarify the role of the rhenium catalyst and MS4A in the Diels−Alder reactions. The yields are as follows: no catalyst 53%; $[ReBr(CO)_3(thf)]_2$ (2.5 mol %) 80%; $[ReBr(CO)_3(thf)]_2$ (2.5 mol %) + MS4A (200 wt%-Re cat.) 64%; and MS4A (200 wt%-Re cat.) 40%. These results show that a rhenium catalyst, $[ReBr(CO)_3(thf)]_2$, accelerated the Diels−Alder reaction between **8b** and **9a**, whereas MS4A slightly inhibited the Diels−Alder reaction.

TABLE 2. Rhenium-Catalyzed Synthesis of Multisubstituted Aromatic Compounds 10 from β-Keto Esters 1 and Alkynes 2 and 9[a]

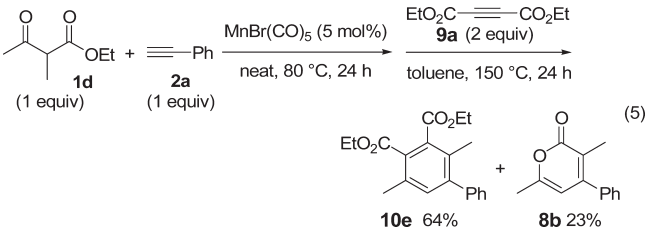


entry	R^1	R^2	compd no.	R^3	R^4	compd no.	R^5	R^6	compd no.	% yield[b]
1	Me	Me	**1d**	Ph	Ph	**2g**	CO_2Et	CO_2Et	**9a**	**10a** 83 (88)
2	Ph	Me	**1e**	Ph	Ph	**2g**	CO_2Et	CO_2Et	**9a**	**10b** 64 (67)
3	Me	H	**1a**	Ph	Ph	**2g**	CO_2Et	CO_2Et	**9a**	**10c** 84 (89)
4	Me	Me	**1d**	Me	Ph	**2h**	CO_2Et	CO_2Et	**9a**	**10d** 91 (92)
5	Me	Me	**1d**	H	Ph	**2a**[c]	CO_2Et	CO_2Et	**9a**[d]	**10e** 87 (93)
6	Me	Me	**1d**	H	Ph	**2a**[e]	CO_2Et	CO_2Et	**9a**[d]	**10e** 80 (85)
7	Me	Me	**1d**	H	Ph	**2i**[f]	CO_2Et	CO_2Et	**9a**[d]	**10f** 72 (77)
8	Me	Me	**1d**	H	Ph	**2i**[e]	CO_2Et	CO_2Et	**9a**[d]	**10f** 66 (71)
9	Me	$^nC_5H_{11}$	**1f**	$^nC_6H_{13}$	Ph	**2j**	CO_2Et	CO_2Et	**9a**	**10g** + **10h** 85 (89) [**10g**:**10h** = 96:4][g]
10	$^nC_5H_{11}$	Me	**1g**	$^nC_6H_{13}$	Ph	**2j**	CO_2Et	CO_2Et	**9a**	**10g** + **10h** 83 (89) [**10g**:**10h** = 6:94][g]
11	Me	Me	**1d**	Ph	Ph	**2g**	CO_2Et	H	**9b**	**10i** 86 (89)
12	Ph	Me	**1e**	Ph	Ph	**2g**	CO_2Et	H	**9b**	**10j** + **10k** 77 (81) [**10j**:**10k** = 39:61][h]

[a] **1** (1 equiv), **2** (1.2 equiv), **9** (2 equiv). [b] Yield determined by ^1H NMR is reported in parentheses. [c] 80 °C, 8 h; 180 °C, 16 h. [d] **9a** (1 equiv, 3 times) was added every 8 h. [e] 80 °C, 8 h. Then, TBAF (10 mol %) was added, and the mixture was stirred at 25 °C for 8 h. [f] 48 h. [g] The ratio of **10g** and **10h** is given in square brackets. [h] The ratio of **10j** and **10k** is given in square brackets.



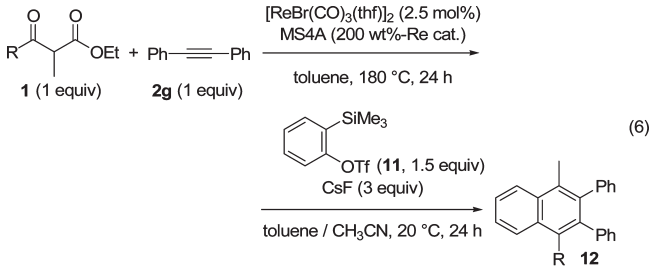
pentasubstituted aromatic compound **10e** was obtained in 64% yield by the reaction of β-keto ester (**1d**) with phenylacetylene (**2a**) in the presence of a catalytic amount of $MnBr(CO)_5$ followed by treatment with alkyne **9a** (eq 5).[15] In this reaction, 2-pyranone **8b**, which is an intermediate of **10e**, remained in 23% yield (eq 5). However, 2-pyranones were not formed when internal alkynes were used instead of **2a**.



(5)

The differences between rhenium and manganese catalysts in the formation of 2-pyranones are summarized as follows: (1) In the case of terminal aryl alkynes, a manganese catalyst, $MnBr(CO)_5$, shows a higher catalytic activity compared with a rhenium catalyst, $[ReBr(CO)_3(thf)]_2$. (2) In other cases, such as terminal aliphatic alkynes and internal alkynes, the rhenium catalyst has a higher catalytic activity (the manganese catalyst promoted the formation of 2-pyranones from terminal aliphatic alkynes in low yields, and did not produce 2-pyranones when internal alkynes were employed).

Synthesis of naphthalene derivatives **12** could be achieved in excellent yields under mild conditions by applying a rhenium-catalyzed reaction (eq 6). Treatment of β-keto ester **1d**, **1e**, or **1g** with alkyne **2g** in the presence of a rhenium catalyst, $[ReBr(CO)_3(thf)]_2$, produced the corresponding 2-pyranones **8a**, **8c**, and **8d**. After the formation of the 2-pyranones, a mixture of 2-trimethylsilylphenyl triflate (**11**) and cesium fluoride was added without isolation of **8a**, **8c**, and **8d**. As a result, tetrasubstituted naphthalene derivatives **12a**, **12b**, and **12c** were produced in 83−96% yields.



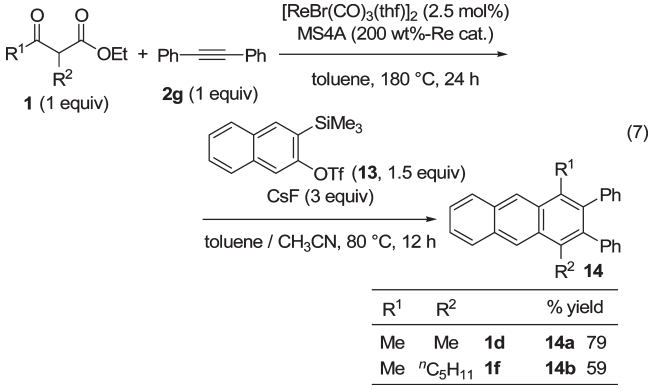
(6)

R		% yield
Me	**1d**	**12a** 92
Ph	**1e**	**12b** 96
$^nC_5H_{11}$	**1g**	**12c** 83

Anthracene derivative **14a** was also generated in 79% yield by treatment with a mixture of 2-(trimethylsilyl)-naphthalen-3-yl trifluoromethanesulfonate (**13**) and cesium fluoride instead of **11** and cesium fluoride after the formation of 2-pyranone **8a** (eq 7). When β-keto ester **1f** was treated with diphenylacetylene (**2g**), the corresponding

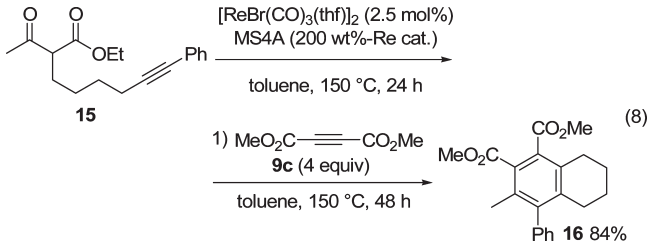
(15) In the first step of the reaction, 2-pyranone **8b** was formed in 96% yield.

anthracene derivative **14b** was produced in 59% yield (eq 7).



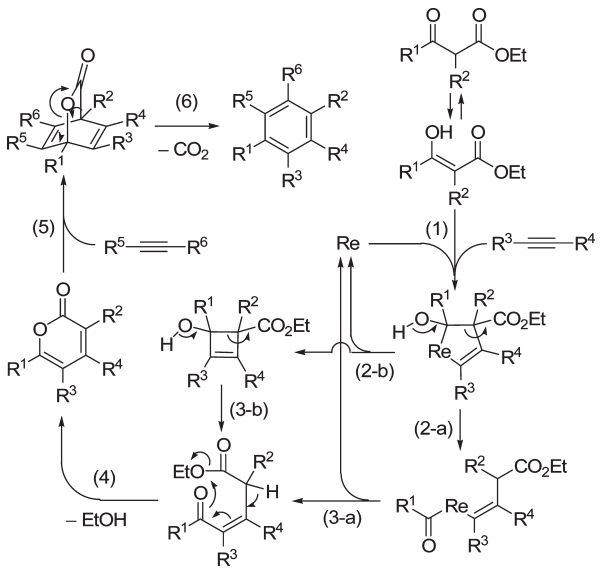
R^1	R^2		% yield
Me	Me	**1d**	**14a** 79
Me	$^nC_5H_{11}$	**1f**	**14b** 59

Intramolecular reaction could also be used to synthesize multisubstituted bicyclic aromatic compounds. By the reaction of a β-keto ester with an acetylene moiety, **15**, using a rhenium catalyst, $[ReBr(CO)_3(thf)]_2$, followed by treatment with alkyne **9c**, tetrahydronaphthalene derivative **16** was afforded in 84% yield (eq 8). This reactivity is in sharp contrast to other intramolecular additions of β-keto esters to alkynes, such as transition metal-catalyzed Conia-ene reactions.[16]

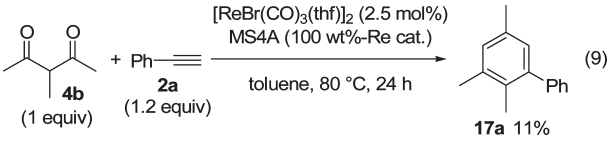


The proposed reaction mechanism is as follows (Scheme 4): (1) formation of a rhenacyclopentene intermediate by a reaction between a rhenium catalyst, β-keto ester, and alkyne (in this step, the β-keto ester and alkyne orient regioselectively); (2, 3) after the formation of the rhenacyclopentene intermediate, a δ-keto ester is generated via (2-a and 3-a) carbon−carbon bond cleavage via a retro-aldol reaction,[17,18] followed by reductive elimination or (2-b and 3-b) a pathway that has a different timing for the reductive elimination;[8,9] (4) isomerization of the olefinic moiety of the δ-keto ester and cyclization leading to 2-pyranone;[19] (5) Diels−Alder reaction between 2-pyranone and the second alkyne; and (6) decarboxylation.

SCHEME 4. Proposed Mechanism for the Formation of Multisubstituted Aromatic Compounds



Rhenium-Catalyzed Synthesis of Tri-, Tetra-, and Pentasubstituted Aromatic Compounds via Carbon−Carbon Bond Cleavage. When 1,3-ketones were employed as substrates instead of the β-keto esters used in eq 4, the products were changed dramatically. Treatment of 1,3-diketone **4b** with phenylacetylene (**2a**) in the presence of a catalytic amount of $[ReBr(CO)_3(thf)]_2$ and molecular sieves afforded tetrasubstituted aromatic compound **17a** in 11% yield (eq 9). Since there are many side products, the yield of **17a** was low. In the side products, a tetrasubstituted acetophenone derivative **5** and deacylated aromatic compound **6** were detected by GC-MS. This result shows that the [2+2+2] type reaction shown in eq 2 also proceeded. In this reaction, a rhenium complex, $Re_2(CO)_{10}$, and manganese complexes, $MnBr(CO)_5$ and $Mn_2(CO)_{10}$, did not show similar catalytic activities.



When *p*-methoxyphenylacetylene (**2b**) was used, tetrasubstituted aromatic compound **17b** was formed in 11% yield (Table 3, entry 1).[20] By the reactions of 1,3-diketone with a phenyl group, **4c**, or without any substituent at the active methylene moiety, **4a**, with *p*-methoxyphenylacetylene (**2b**), biaryl compounds **17c** and **17d** were provided in 22% and 17% yields, respectively (Table 3, entries 2 and 3). By using diphenylacetylene (**2g**), the yield of the aromatic compound increased, and pentasubstituted aromatic compound **17e** was afforded in 43% yield (Table 3, entry 4). However, the reaction did not occur with 6-dodecyne.

If the reaction proceeds between 1 equiv of 1,3-diketones and 1 equiv of alkynes, then there is one extra carbon

(16) For examples of transition metal-catalyzed Conia-ene reactions, see: (a) Kennedy-Smith, J. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 4526. (b) Gao, Q.; Zheng, B.-F.; Li, J.-H.; Yang, D. *Org. Lett.* **2005**, *7*, 2185. (c) Tsuji, H.; Yamagata, K.-i.; Itoh, Y.; Endo, K.; Nakamura, M.; Nakamura, E. *Angew. Chem., Int. Ed.* **2007**, *46*, 8060. (d) Deng, C.-L.; Song, R.-J.; Guo, S.-M.; Wang, Z.-Q.; Li, J.-H. *Org. Lett.* **2007**, *9*, 5111. See also ref 5.

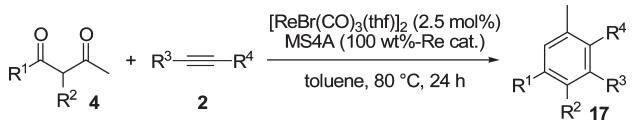
(17) There have been some examples on chemical transformations via carbon−carbon bond cleavage. See: (a) Murakami, M.; Ito, Y. (Murai, S., Ed.) *Top. Organomet. Chem.* **1999**, *3*, 97. (b) Jun, C.-H. *Chem. Soc. Rev.* **2004**, *33*, 610.

(18) (a) Kochetkov, N. K.; Kudryashov, L. J.; Gottich, B. P. *Tetrahedron* **1961**, *12*, 63. (b) Crombie, L.; James, A. W. G. *Chem. Commun* **1966**, 357.

(19) (a) Fried, J.; Elderfield, R. C. *J. Org. Chem.* **1941**, *6*, 566. (b) Wiley, R. H.; Jarboe, C. H.; Hayes, F. N. *J. Am. Chem. Soc.* **1957**, *79*, 2602.

(20) The structure of **17b** was determined by the comparison with the spectrum data of **17b**, which was prepared by palladium-catalyzed cross-coupling reaction between 4-methoxyphenylboronic acid and 2,3,5-trimethylphenyl trifluoromethanesulfonate.

TABLE 3. Reactions between 1,3-Diketones 4 and Alkynes 2[a]

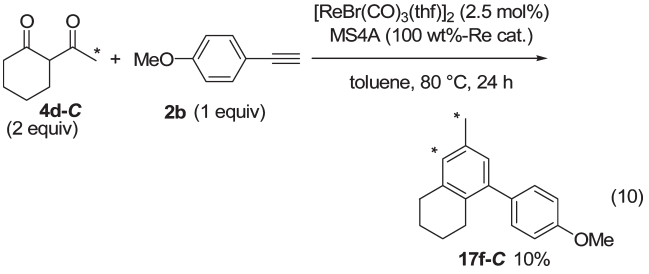


entry	1,3-diketone	alkyne	product	% yield[b]
1[c]	**4b**	**2b**	**17b**	11 (19)
2[c]	**4c**	**2b**	**17c**	22 (38)
3[c]	**4a**	**2b**	**17d**	17 (25)
4[d]	**4b**	**2g**	**17e**	43 (59)

[a] **4** (2 equiv), **2** (1 equiv). [b] Yield determined by ^{1}H NMR is reported in parentheses. [c] **4** (1 equiv), **2** (1.2 equiv). [d] MS4A (200 wt %-Re cat.), 150 °C.

atom in the biaryl products. To elucidate the source of the one carbon atom, we examined the following ^{13}C labeling experiment.

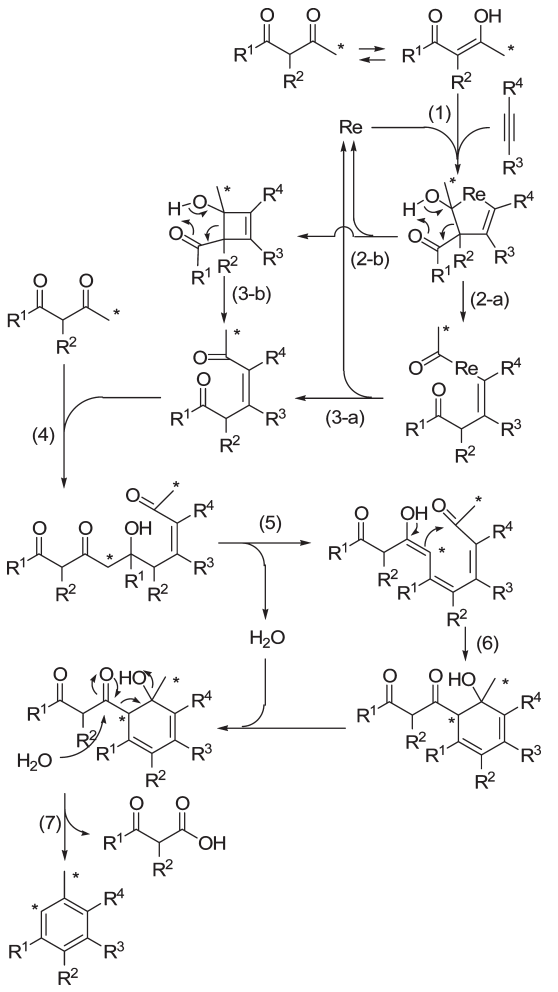
^{13}C labeled 1,3-dicarbonyl compound **4d-*C*** was employed (eq 10). Interestingly, biaryl product **17f-*C*** contained two ^{13}C enriched carbon atoms. This result indicates that a methyl carbon of the 1,3-dicarbonyl compounds (see the structure of **4d-*C***) is the source of the additional carbon atom.



From the ^{13}C labeling experiments and the positions of substituents at the substrates and products, the proposed reaction mechanism is as follows (Scheme 5): (1) formation of a rhenacyclopentene intermediate from a 1,3-diketone, alkyne, and rhenium; (2, 3) after the formation of the rhenacyclopentene intermediate, there are two possible pathways, the difference is the timing of reductive elimination: Path A: (2-a) retro-aldol reaction and (3-a) reductive elimination to give unsaturated 1,5-diketone; Path B: (2-b) reductive elimination and (3-b) retro-aldol reaction to give unsaturated 1,5-diketone; (4) aldol reaction between

(21) In Scheme 5, the formation of β-keto acid was not detected by GC. The β-keto carboxylic acid might be decomposed (Krapcho reaction) or reacted with a species before decomposition under the reaction conditions. Therefore, the generation of β-keto carboxylic acid is only speculated.

SCHEME 5. Proposed Mechanism for the Formation of Aromatic Compounds 17



the unsaturated 1,5-diketone and another 1,3-diketone; (5) dehydration; (6) intramolecular aldol reaction; and (7) elimination of β-keto carboxylic acid to give multisubstituted aromatic compounds.[21]

Conclusion

We have succeeded in the synthesis of aromatic compounds using three different methods. The first approach is a manganese-catalyzed [2+2+2] cycloaddition between 1,3-dicarbonyl compounds and 2 equiv of terminal alkynes. In this reaction, two substituents of the alkynes locate on 1,4-positions of the formed aromatic skeletons regioselectively. The second is a rhenium- and manganese-catalyzed formal [2+1+2+1] cycloaddition reaction of β-keto esters and two kinds of alkynes. The first alkynes insert into a carbon−carbon single bond of β-keto esters regioselectively, and successive intramolecular cyclization provides 2-pyranone derivatives. The 2-pyranones can act as diene components, and react with the second alkynes in a Diels−Alder fashion to give multisubstituted aromatic compounds regioselectively. The third approach is a rhenium-catalyzed formal [2+2+1+1] cycloaddition between 1,3-diketones and alkynes. In this reaction, aromatic compounds are derived from 1,3-diketones, alkynes, and a part of another

1,3-diketone. Interestingly, aromatic compounds can be synthesized by three different means whereas these three reactions employ 7 group transition metal catalysts and similar substrates, which are 1,3-dicarbonyl compounds and alkynes. We hope that these methods will become powerful tools to synthesize multisubstituted aromatic compounds.

Experimental Section

Synthesis of 3′-Methyl[1,1′;4′,1″]terphenyl-2′-carboxylic Acid Ethyl Ester (3a). A mixture of β-keto ester **1a** (32.5 mg, 0.250 mmol), phenylacetylene (**2a**, 63.8 mg, 0.625 mmol), $MnBr(CO)_5$ (3.4 mg, 0.0125 mmol), and molecular sieves 4A (3.9 mg, 115 wt %-Mn cat.) was stirred at 80 °C for 24 h. After the reaction was quenched with a solution of HCl in ether (0.25 mL), the solvent was removed in vacuo. The product was isolated by column chromatography on silica gel (hexane:ethyl acetate = 20:1) to give **3a** in 85% yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (t, J = 7.2 Hz, 3H), 2.28 (s, 3H), 4.08 (q, J = 7.2 Hz, 2H), 7.26−7.46 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 17.6, 61.0, 127.0, 127.1, 127.4, 128.17, 128.21, 128.4, 129.3, 130.8, 132.4, 134.4, 139.0, 140.7, 141.1, 141.7, 170.0; IR (Nujol/cm^{-1}) 1719, 1302, 1246, 1173, 1144, 1067, 1007, 835, 766, 721, 700; HR-MS calcd for $C_{22}H_{20}O_2$ (M^+) 316.1463, found 316.1452.

Selective Synthesis of 5. A mixture of 2,4-pentanedione (**4**, 25.0 mg, 0.250 mmol), phenylacetylene (**2a**, 63.8 mg, 0.625 mmol), $MnBr(CO)_5$ (3.4 mg, 0.0125 mmol), molecular sieves 4A (3.9 mg, 115 wt %-Mn cat.), and toluene (0.50 mL) was stirred at 50 °C for 24 h. After the solvent was removed in vacuo, the product was isolated by column chromatography on silica gel (hexane:ethyl acetate = 20:1) to give **5** in 69% yield as a white solid.

Selective Synthesis of 6. A mixture of 2,4-pentanedione (**4**, 25.0 mg, 0.250 mmol), phenylacetylene (**2a**, 63.8 mg, 0.625 mmol), $MnBr(CO)_5$ (3.4 mg, 0.0125 mmol), $Sc(OTf)_3$ (6.2 mg, 0.0125 mmol), toluene (0.25 mL), and water (0.25 mL) was stirred at 80 °C for 24 h. After the solvent was removed in vacuo, the product was isolated by column chromatography on silica gel (hexane:ethyl acetate = 10:1) to give **6** in 68% yield as a white solid.

Synthesis of 3,6-Dimethyl-4,5-diphenylpyran-2-one (8a). A mixture of ethyl 2-methylacetoacetate (**1d**, 72.1 mg, 0.500 mmol) and diphenylacetylene (**2g**, 107 mg, 0.600 mmol) in the presence of $[ReBr(CO)_3(thf)]_2$ (10.6 mg, 0.0125 mmol) and powdered MS4A (21.2 mg, 200 wt %-Re cat.) in toluene (1.0 mL) was heated at 180 °C for 24 h under argon atmosphere. After purification by silica gel column chromatography, 3,6-dimethyl-4,5-diphenylpyran-2-one (**8a**) was obtained in 96% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.92 (s, 3H), 2.12 (s, 3H), 6.86−6.90 (m, 4H), 7.12−7.17 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 18.5, 119.2, 119.4, 127.1, 127.5, 127.8, 127.9, 128.2, 130.4, 135.2, 136.5, 154.0, 155.6, 164.0; IR (Nujol/cm^{-1}) 3086, 3062, 3027, 2921, 2859, 1733, 1718, 1653, 1457, 1379, 1041, 896. Anal. Calcd for $C_{19}H_{16}O_2$: C, 82.58; H, 5.84. Found: C, 82.46; H, 5.90.

Typical Procedure for the Synthesis of Multisubstituted Benzenes from β-Keto Esters and Two Alkynes. Diethyl 3,6-Dimethyl-4,5-diphenylphthalate (10a). A mixture of ethyl 2-methylacetoacetate (72.1 mg, 0.500 mmol) and diphenylacetylene (107 mg, 0.600 mmol) in the presence of $[ReBr(CO)_3(thf)]_2$ (10.6 mg, 0.0125 mmol) and powdered MS4A (21.2 mg, 200 wt %-Re cat.) in toluene (1.0 mL) was heated at 180 °C under argon atmosphere. After 24 h, acetylene dicarboxylic acid ethyl ester (170 mg, 1.00 mmol) was added. The reaction mixture was stirred at 150 °C for 24 h. After purification by silica gel column chromatography, diethyl 3,6-dimethyl-4,5-diphenylphthalate (**10a**) was obtained in 83% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (t, J = 7.2 Hz, 6H), 2.08 (s, 6H), 4.38 (q, J = 7.2 Hz, 4H), 6.88 (d, J = 7.8 Hz, 4H), 7.05−7.14 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 18.6, 20.7, 126.1, 127.5, 129.4, 130.0, 133.4, 140.2, 144.8, 168.6; IR (Nujol/cm^{-1}) 3060, 3011, 2924, 2855, 1727, 1600, 1568, 1479, 1072, 964, 752, 727, 625. Anal. Calcd for $C_{26}H_{26}O_4$: C, 77.59; H, 6.51. Found: C, 77.44; H, 6.54.

Preparation of Naphthalene Derivatives. 1,4-Dimethyl-2,3-diphenylnaphthalene (12a). A mixture of ethyl 2-methylacetoacetate (**1d**, 72.1 mg, 0.500 mmol) and diphenylacetylene (**2g**, 107 mg, 0.600 mmol) in the presence of $[ReBr(CO)_3(thf)]_2$ (10.6 mg, 0.0125 mmol) and powdered MS4A (21.2 mg, 200 wt %-Re cat.) in toluene (1.0 mL) was heated at 180 °C under argon atmosphere. After 24 h, 2-(trimethylsilyl)phenyl triflate (**11**, 223.8 mg, 0.750 mmol), cesium fluoride (228 mg, 1.50 mmol), and acetonitrile (1.0 mL) were added. The reaction mixture was stirred at 20 °C for 24 h. After purification by silica gel column chromatography, 1,4-dimethyl-2,3-diphenylnaphthalene (**12a**) was obtained in 91% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 6H), 6.95−6.98 (m, 4H), 7.07−7.14 (m, 6H), 7.57−7.60 (m, 2H), 8.13−8.16 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.9, 125.0, 125.7, 125.8, 127.2, 129.4, 130.4, 132.0, 139.4, 141.7; IR (Nujol/cm^{-1}) 3055, 3011, 2928, 2860, 1456, 1377, 1070, 916, 851, 750, 702, 599; Anal. Calcd for $C_{24}H_{20}$: C, 93.46; H, 6.54. Found: C, 93.23; H, 6.64.

Preparation of Anthracene Derivatives. 1,4-Dimethyl-2,3-diphenylanthracene (14a). A mixture of ethyl 2-methylacetoacetate (**1d**, 72.1 mg, 0.500 mmol) and diphenylacetylene (**2g**, 107 mg, 0.600 mmol) in the presence of $[ReBr(CO)_3(thf)]_2$ (10.6 mg, 0.0125 mmol) and powdered MS4A (21.2 mg, 200 wt %-Re cat.) in toluene (1.0 mL) was heated at 180 °C under argon atmosphere. After 24 h, 2-(trimethylsilyl)naphthalen-3-yl trifluoromethanesulfonate (**13**, 261.3 mg, 0.750 mmol), cesium fluoride (228 mg, 1.50 mmol), and acetonitrile (1.0 mL) were added. The reaction mixture was stirred at 80 °C for 12 h. After purification by silica gel column chromatography, 1,4-dimethyl-2,3-diphenylanthracene (**14a**) was obtained in 91% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.66 (s, 6H), 7.09−7.11 (m, 4H), 7.18−7.26 (m, 6H), 7.56−7.59 (m, 2H), 8.13−8.15 (m, 2H), 8.76 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.2, 123.7, 125.4, 125.9, 127.2, 128.3, 130.4, 130.9, 131.5, 138.8, 141.8; IR (Nujol /cm^{-1}) 2723, 1599, 1460, 1376, 1211, 1030, 872, 722, 700, 665. Anal. Calcd for $C_{28}H_{22}$: C, 93.81; H, 6.19. Found: C, 93.77; H, 6.28.

Intramolecular Reaction. Dimethyl 3-Methyl-4-phenyl-5,6,7,8-tetrahydronaphthalene-1,2-dicarboxylate (16). A mixture of ethyl 2-acetyl-8-phenyloct-7-ynoate (**15**, 143 mg, 0.500 mmol), $[ReBr(CO)_3(thf)]_2$ (10.6 mg, 0.0125 mmol), and powdered MS4A (10.6 mg, 100 wt %-Re cat.) in toluene (2.0 mL) was heated at 150 °C under argon atmosphere for 24 h. Then, an acetylene dicarboxylic acid methyl ester (**9c**, 142 mg, 1.00 mmol) was added and the mixture was stirred at 150 °C. After 24 h, an additional acetylene dicarboxylic acid methyl ester (**9c**, 142 mg, 1.00 mmol) was added and the mixture was heated at 150 °C for 24 h. After purification by silica gel column chromatography, dimethyl 3-methyl-4-phenyl-5,6,7,8-tetrahydronaphthalene-1,2-dicarboxylate (**16**) was obtained in 84% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.62−1.66 (m, 2H), 1.68−1.74 (m, 2H), 1.98 (s, 3H), 2.29 (t, J = 6.3 Hz, 2H), 2.83 (t, J = 6.3 Hz, 2H), 3.86 (s, 3H), 3.89 (s, 3H), 7.05 (d, J = 6.9 Hz, 2H), 7.34−7.38 (m, 1H), 7.42−7.46 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.94, 22.28, 22.52, 27.30, 29.32, 52.26, 52.28, 127.06, 128.57, 128.77, 129.55, 131.34, 131.75, 132.99, 138.63, 140.08, 144.71, 169.16, 169.20; IR (Nujol/cm^{-1}) 3051, 2930, 2852, 1725, 1568, 1435, 1126, 1028, 958, 846, 794, 731, 704, 609. Anal. Calcd for $C_{21}H_{22}O_4$: C, 74.54; H, 6.55. Found: C, 74.77; H, 6.60.

Typical Procedure for Rhenium-Catalyzed Synthesis of Multisubstituted Aromatic Compounds from 1,3-Diketones and Alkynes. 1,3,4-Trimethyl-5-phenylbenzene (17a). A mixture of 3-methyl-2,4-pentanedione (**4b**, 57.1 mg, 0.500 mmol) and phenylacetylene (**2a**, 61.3 mg, 0.600 mmol) in the presence of $[ReBr(CO)_3(thf)]_2$ (10.6 mg, 0.0125 mmol) and powdered MS4A (21.2 mg, 100 wt %-Re cat.) in toluene (1.0 mL) was heated at 80 °C under argon atmosphere for 24 h. After purification by silica gel column chromatography, 1,3,4-trimethyl-5-phenylbenzene (**17a**) was obtained in 11% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (s, 3H), 2.33 (s, 6H), 6.94 (s, 1H), 7.02 (s, 1H), 7.30−7.35 (m, 3H), 7.39−7.43 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.5, 20.6, 20.8, 126.5, 127.9, 128.3, 129.4, 129.7, 130.8, 134.5, 137.0, 142.2, 142.7; IR (neat /cm^{-1}) 3028, 2918, 2862, 1601, 1576, 1495, 1474, 1456, 1382, 1072, 1009, 858, 773, 758, 702, 646, 584. Anal. Calcd for $C_{15}H_{16}$: C, 91.78; H, 8.22. Found: C, 91.94; H, 8.12.

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Supporting Information Available: The general procedure, product characterization data for **3b**−**h**, **5**, **6**, **10b**−**k**, **12b**,**c**, **14b**, and **17b**−**f**, and ^{1}H and ^{13}C NMR spectra of **3a**−**h**, **5**, **6**, **8**, **10a**−**k**, **12a**−**c**, **14a**,**b**, **16**, and **17a**−**f**. This material is available free of charge via the Internet at http://pubs.acs.org.