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Rhodium-Catalyzed Synthesis of Eight-Membered Rings

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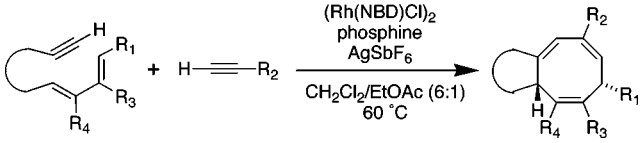

Experiments to develop a rhodium catalyst for the [4 + 2 + 2] cycloisomerization of dienynes with a second alkyne are described. The generality of the reaction is probed in terms of dienyne structure and alkyne structure. A catalyst system that provides cyclooctatrienes in greater than 70% yield is reported. Several experiments to determine the nature of the catalyst are described.

Introduction

Over the last 30 years, several workers have achieved moderate success performing intermolecular metal-catalyzed [4 + 2] cyclodimerizations.[1−9] In 1994, McKinstry and Livinghouse reported the highly successful rhodium-catalyzed intramolecular [4 + 2] cycloisomerization of trienes and dienynes.[10−12] While functionally analogous to the Diels-Alder reaction, the rhodium-catalyzed cycloisomerization does not require the HOMO−LUMO matching necessary in either the thermal or Lewis acid catalyzed cycloaddition. Inspired by the Livinghouse work, we reported a cationic rhodium catalyst system that is highly effective and in many cases provides high asymmetric selectivity in this reaction (Scheme 1).[13,14] During the work on the asymmetric system, using DuPHOS as the phosphine ligand on the rhodium, the formation of a product resulting from the dimerization of the dienyne was observed (Scheme 1). This paper reports the details of the development of a catalyst system optimized for dimer formation, the development of a cross-reaction between a dienyne and another alkyne, and work to examine the generality of the reaction. Independent of our work, Evans and co-workers developed a

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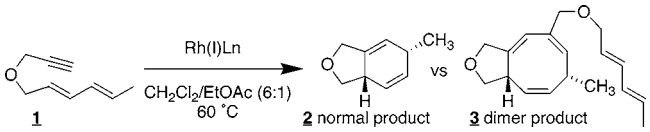
SCHEME 1



comparable approach to eight-membered rings using enynes and butadiene.[15−21]

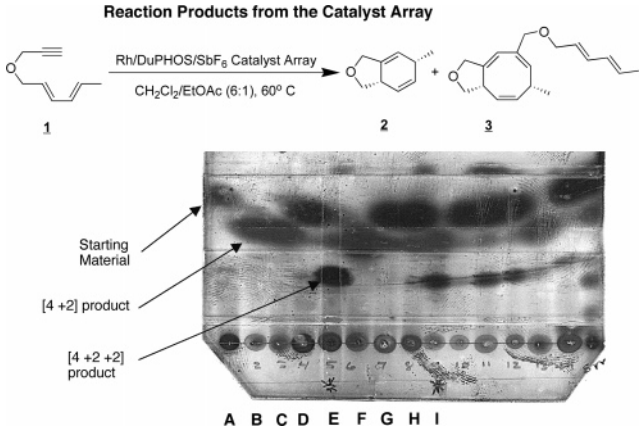
Dimer **3**, the byproduct of the [4 + 2] cycloisomerization, is rich in functionality, containing an eight-membered ring with three double bonds. During the course of our [4 + 2] cycloisomerization work, this product was observed sporadically. Because of its interesting structure, an attempt was made to develop a system that consistently provided this product. Considerable work, examining different solvents, temperatures, and reagent ratios, resulted in inconsistent results, however, ultimately an approach to systematically screen rhodium species resulted in the discovery of an effective catalyst system for this transformation.

Results and Discussion

The formulation of the catalyst was arrived at through a systematic screen of different reagent ratios for the formation of the catalyst system. Utilizing a method previously employed by researchers such as Morken and co-workers,[22,23] Stambuli et al.,[24] and Reetz and co-workers,[25−27] an array of catalysts, each made with differing ratios of metal ligand and silver salt, was tested. To avoid removal of minor species that may be responsible for the desired product, the potential catalysts were used without purification. Table 1 contains the ratios of the reagents that were used for catalyst generation and qualitatively illustrates the results of these catalysts' reactions with dienyne, **1** (10 mol % catalyst, on the basis of Rh). As can be seen by the thin-layer chromatography (TLC) in Table 1, we found that reaction of $[Rh(NBD)Cl]_2$ with one-half of an equivalent, or less (on the basis of rhodium), of $AgSbF_6$ in the presence of Me-DuPHOS provided a catalyst system that upon heating to 60 °C with the substrate gave the desired product in good to excellent yield (Table 1, **E** and **I**).

TABLE 1. Array of Catalysts Synthesized

catalyst number	equivalents of $[Rh(NBD)Cl]_2$	equivalents of Me-DuPHOS	equivalents of $AgSbF_6$
cat **A**	1	1	0
cat **B**	1	1	1
cat **C**	1	1	2
cat **D**	1	2	0
cat **E**	1	2	1
cat **F**	1	2	2
cat **G**	1	3	0
cat **H**	1	3	1
cat **I**	1	3	2



As shown in the TLC in Table 1, catalysts **A** and **D** failed to produce either the [4 + 2] or the [4 + 2 + 2] dimer, while catalysts **B**, **C**, and **F** exclusively produced the [4 + 2] cycloadduct. Complexes **E** and **I** were the only catalysts that produced the [4 + 2 + 2] product, **3**, in 76% and 23% yield, respectively. On the basis of this experiment, it was decided to use $[Rh(NBD)Cl]_2$ with one-half of an equivalent, or less (on the basis of rhodium), of $AgSbF_6$ in the presence of Me-DuPHOS as the catalyst system.

With an effective catalyst system, the scope of the reaction was probed with several substrates. As illustrated in Table 2, both 3- and 4-atom tethers can be effective, giving either the [6.3.0] or [6.4.0] ring systems. Tethers containing either oxygen or nitrogen, as the sulfonamide, were effective. When substrates where the diene does not have a terminal alkyl group are used, two regioisomers, resulting from the incorporation of the alkyne in two orientations, can be obtained (Table 2 entry 2). However, in the case of entry 4, only one regioisomer was observed.

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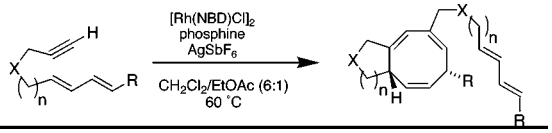
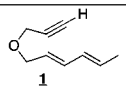
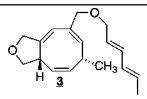
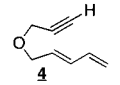
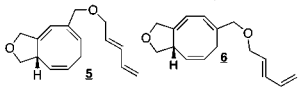
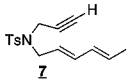
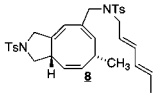
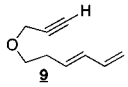
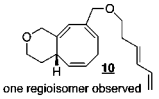
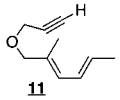
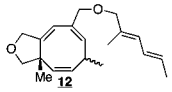
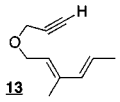
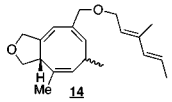
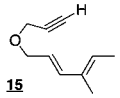
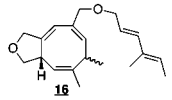
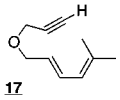
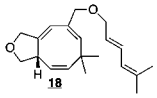
TABLE 2. Dimer Formation[a]



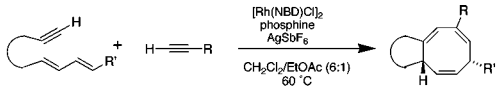
Entry No.	Dienyne	Yield	Product
1[a]		80%[c]	
2[a]		44%[c]	
3[b]		72%[c]	
4[b]		58%	
5		0%	
6		10%[d]	
7		61%[d]	
8		0%	

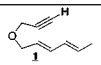
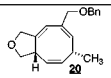
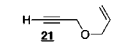
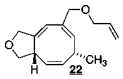
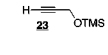
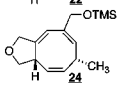
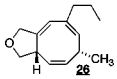
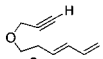
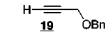
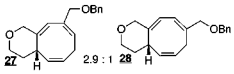
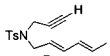
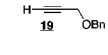
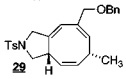
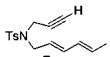
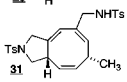
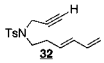
[a] The catalyst was generated from a ratio of 1:2:1 of $[Rh(NBD)Cl]_2$:DuPHOS:$AgSbF_6$ and was run in CH_2Cl_2:EtOAc (6:1). Reaction was run at room temperature approximately 12 h. [b] Reaction was run at 60 °C, approximately 12 h. [c] The products were isolated as single diastereomers. [d] Stereochemistry assigned by analogy to earlier examples.

In the case where the diene section of the dienyne is substituted with a methyl group, the yields vary from 0 to 60% (entries 5−8). When either end of the diene is disubstituted (entries 5 and 8), only starting material is recovered from the reaction. Neither the [4 + 2 + 2] nor the [4 + 2] reactions take place. In the case where the diene is substituted in the 3 position, a 10% yield of the [4 + 2 + 2] product is obtained with 23% of the [4 + 2] product also isolated. The highest yield (61%) was obtained when the methyl group is in the 2-position of the diene (entry 7). While on the basis of steric arguments it is easy to rationalize why the substrates that are disubstituted on the ends (**11** and **17**) do not react, it is not so clear why **13** with the internal methyl does not participate well in the [4 + 2 + 2] reaction. One reason for the low yield with substrate **13** may be the steric interaction between the methyl group and the methylene next to the oxygen tether. Steric crowding between the methyl and the CH_2 may prevent the planar geometry necessary for closure.

While dimer formation was used as a model to optimize the reaction conditions, it was desirable to insert a different alkyne during the reaction. Table 3 illustrates that such a cycloisomerization cross-coupling reaction is indeed possible. When the cycloisomerization reaction is run in the presence of 5 equiv of a second alkyne, the desired cross-coupled-cyclized product is obtained (Table 3).

TABLE 3. [4 + 2 + 2] Cyclization with Incorporation of a Second Alkyne



Entry[a]	Dienyne	Alkyne	Yield	Product
1			73%[b]	
2			36%[b]	
3			63%[b]	
4			41%[b]	
5			55%	
6			70%[b]	
7			49%[b]	
8			69%	
9			43%	
10			0%	
11			10%[d]	
12			64%[d]	
13			0%	
14			62%[d]	
15			63%[d]	
16			64%[d]	

[a] The catalyst was generated from a ratio of 1:2:1 of $[Rh(NBD)Cl]_2$:DuPHOS:$AgSbF_6$ and was run in CH_2Cl_2:EtOAc (6:1). Reaction was run at room temperature approximately 12 h. [b] The products were isolated as single diastereomers. [c] Reactions where run following bubbling acetylene gas through the solvent while cooling to 0 °C. [d] The products where isolated as single diastereomers and the stereochemistry was assigned by analogy to earlier examples.

In addition to ether and sulfonamide tethers, carbon tethers, in the form of an aromatic ring (entry 9), were also found to be useful. When the nitrogen in the tether is protected as its acetamide, no product was observed. Many different alkynes are accepted. While simple terminal alkyl acetylenes will provide the desired product (Table 3 entry 4), there appears to be a

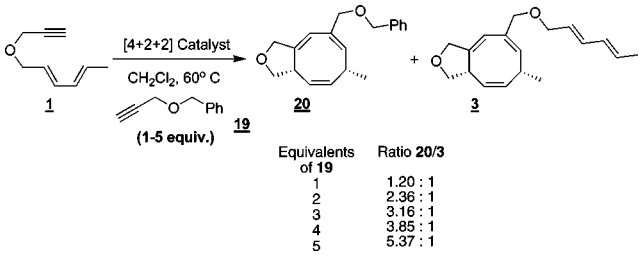


FIGURE 1. [4 + 2 + 2] Cocyclizations with various amounts of the auxiliary alkyne.

preference for propargyl ethers, with propargylbenzyl ether generally giving the highest yields. Toluene sulfonamide protected propargyl amine also provided the desired product (Table 3 entry 7). Reaction with propargyl alcohol did not proceed and attempted reaction with 3-hexyne or phenyl acetylene gave only product from dimerization of the dienyne. The substrates that possess methyl substituents on the diene provided the same reactivity profile in the cross-coupling cyclization as with dimer formation with only the dienyne possessing a methyl group in the 2-position of the diene providing the desired product in acceptable yield (64%, entry 12).

In addition to proceeding with terminal alkynes, the reaction runs well with acetylene. The reaction of dienynes **1**, **13**, and **15** proceeds to provide the expected product in greater than 60% yield. The reaction is run by simply bubbling acetylene into the reaction solution prior to sealing the Schlenk tube and heating.

The stereochemical control in the reaction system is interesting. In all the cases where the diene has a terminal methyl group, only one diastereomer of the product has been observed. In our work with asymmetric [4 + 2] cycloisomerizations, we have found that Me-DuPHOS is effective in transferring its chirality to the products of simple dieneynes.[13,14] This is not the case with the catalyst system developed here. The highest selectivity observed in these reactions was in Table 3 entry 3 (41% ee).

A study was performed in which the amount of the auxiliary alkyne was varied to determine the dependence of the quantity of the alkyne on the ratio of dimer to cross-coupling products. As can be seen in Figure 1, the ratio of **20** to **3** consistently increases as the ratio of benzyl propargyl ether to dienyne increases. Five equivalents of this terminal alkyne produced a 5.4:1 mixture of the two products. For practical reasons, the reaction was not examined with more than 5 equiv of the alkyne. We have discussed earlier that propargyl ethers appear to be optimal substrates for the incorporation of an alkyne into the reaction. In the study shown in Figure 1, the dienyne **1** and the auxiliary alkyne **19** are both propargyl ethers, and it may be difficult for the catalyst to discriminate between them. Using less similar molecules, that is, a tether that is not a propargyl ether, should diminish the competition between the two substrates and could enhance the reaction's preference for the cocyclized product. Despite the similarity between the dienyne and alkyne, reasonable yields of the [4 + 2 + 2] type product are obtained using only 5 equiv of alkyne. In cases where the alkyne is valuable, its quantity can be reduced to 3 equiv while maintaining a ratio of products of 3:1.

At the present time, we do not know the exact nature of the catalyst system. In our work on the rhodium-catalyzed [4 + 2] reaction, we have generated the catalyst by treatment of $[Rh(NBD)Cl]_2$ with 1 equiv of $AgSbF_6$, on the basis of rhodium, in acetone, which is then added to the appropriate phosphine. This procedure provides a yellow homogeneous solution that is then treated with H_2 or is used as is to catalyze the desired reaction. As stated above, in the system reported here, the catalyst is generated by treatment of a solution of $[Rh(NBD)Cl]_2$ and Me-DuPHOS with one-half of an equivalent or less of $AgSbF_6$ in tetrahydrofuran (THF). Following exchange of the solvent, the catalyst is used after treatment with H_2 gas. Approximately 1 h into the reaction, a dark brown precipitate forms on the walls of the reaction vessel.

Several experiments were performed to identify the active catalyst precursor that was responsible for producing the dimer (**3**). Attempts were made to purify catalysts **E** and **I** (Table 1) by flash chromatography. Four fractions were isolated, but upon treatment of each of these with dienyne **1** none of them produced the desired product, although one fraction did produce the [4 + 2] product.

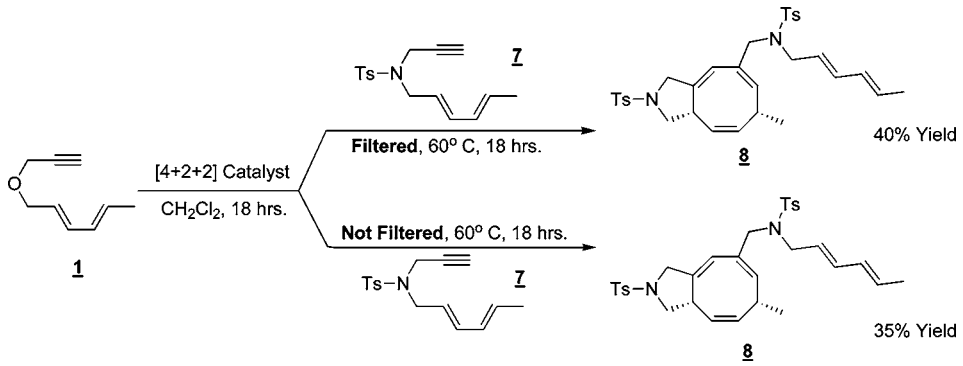
Analysis of Table 1 reveals that the most active catalyst (**E**) contains one bidentate ligand for each atom of rhodium but only one-half of an equivalent of $AgSbF_6$ is present. To see if this exact ratio was necessary, the amount of $AgSbF_6$ was decreased to 25% and 10% of the molar rhodium content. The [4 + 2 + 2] reaction proceeded smoothly with the 25% silver, but only starting material was isolated in the example with 10% $AgSbF_6$. Since insoluble material is formed during the reaction sequence, two experiments were attempted in which $[Rh(NBD)Cl]_2$, in the absence of phosphine, was mixed with 1 and 2 equiv (one-half and 1 equiv on the basis of rhodium) of $AgSbF_6$, respectively. Each of these mixtures was subjected to the reaction conditions and in both cases, only the [4 + 2] cycloadduct (**2**) was observed.

When forming the [4 + 2 + 2] catalyst having the Rh/DuPHOS/SbF_6 ratio of 2:2:1 (**E**), several interesting observations can be made. The initial solution of $[Rh(NBD)Cl]_2$ in THF is orange. Once this solution is mixed with a solution of Me-DuPHOS in THF, an immediate color change from orange to red is observed. After stirring for 15 min, this red solution is mixed with a solution of $AgSbF_6$ (one-half equiv) in THF. After a few minutes, a dark-colored precipitate begins to form. This is in contrast to the white precipitate of AgCl that forms in the [4 + 2] catalyst preparations (1:1:1 stoichiometry). This precipitate is filtered after 15 min using a syringe filter, and the mother liquor is evaporated to dryness. The resulting orange solid is used without further purification. While the reaction mixture starts out homogeneous, during the course of the [4 + 2 + 2] cyclizations, it becomes heterogeneous. It is possible that the [4 + 2 + 2] reaction is catalyzed by a heterogeneous rhodium species and not by the initially formed solution.

The ^{31}P-NMR spectrum of a solution of the "catalyst" shows that the [4 + 2 + 2] catalyst (**E**) contains at least three rhodium-phosphorus species (^{31}P-NMR 120 MHz, $CDCl_3$ δ = 100, 79.2, 78.5). Generally, the ratios of the three species differ from batch to batch of the catalyst. Despite this variation in the ratio of complexes, each batch is a competent catalyst for the desired [4 + 2 + 2] cycloaddition reaction. Consequently, it is not clear which, if any, of the species observed by ^{31}P NMR is responsible for the [4 + 2 + 2] product.

An experiment was designed to determine whether the precipitate was essential for the reaction to proceed. A [4 + 2 + 2] reaction was set up using the ether-linked substrate, **1** (Scheme 2). The reaction proceeded to completion with the

SCHEME 2. Heterogeneous vs Homogeneous Catalysis



reaction mixture appearing dark and heterogeneous. The reaction mixture was then split in two. Half of the reaction mixture was filtered through a syringe filter into a second reaction containing the tosylamide-linked substrate, **7**. The other half of the heterogeneous reaction was mixed with **7** without filtration. The filtered reaction mixture appeared orange and homogeneous, while the unfiltered reaction mixture was heterogeneous and gray/brown colored. Both the filtered and unfiltered versions of the catalyst provided the [4 + 2 + 2] product. A 40% yield of the tosylamide [4 + 2 + 2] dimer (**8**) was obtained from the filtered reaction while a 35% yield was obtained from the control reaction (Scheme 2). This experiment does not conclusively rule out the involvement of small-suspended colloidal particles, but it appears that the precipitate is not likely to be involved in catalyzing the [4 + 2 + 2] reaction.

Conclusions

The cocyclization reaction, using 3−5 equiv of an auxiliary terminal alkyne, proved to be quite general in that a variety of both dienynes and terminal alkynes were readily cocyclized. The system does not tolerate disubstitution at the ends of the diene or internal alkynes, but a variety of linking groups appear to be tolerated, so long as they are sufficiently unreactive. While work to determine the nature of the catalyst was not successful in determining the structure of the catalyst or the precatalyst, the system has been sufficiently developed so that it can consistently be generated and used. Work is presently being done to utilize this reaction in the total synthesis of several natural products.

Experimental Section

Representative Procedure for the Preparation of Catalyst. To a vial containing $[Rh(NBD)Cl]_2$ (75 mg, 0.16 mmol), 2 mL of THF is added. After stirring for 15 min, this orange solution is quickly transferred via cannula to a vial containing a solution of (*S*,*S*)-Me-DuPHOS (98 mg, 0.32 mmol) in 2 mL of THF. After stirring for 15 min, this red solution is transferred via cannula to a vial containing a solution of $AgSbF_6$ (56 mg, 0.16 mmol) in 2 mL of THF. After 15 min, this dark suspension is transferred to a tared vial using a syringe fitted with a filter. The cherry red filtrate is concentrated in vacuo and is kept under vacuum (<1 mmHg) overnight to remove all solvent. Two hundred eleven milligrams of orange/red solid was collected. This catalyst can be stored under nitrogen at 0 °C for a short period of time.

General Procedure for the [4 + 2 + 2] Dimerization of a Dienyne. To a clean, dry 15-mL Schlenk tube, 30 mg of catalyst was added as a solution in 2 mL of CH_2Cl_2. H_2 was gently bubbled through the orange/red solution for 3 min causing it to become dark and cloudy, after which 0.5 mL of EtOAc was added followed by sparging with N_2 for 3 min. The dienyne (0.38 mmol) was then added along with 1 mL of CH_2Cl_2. The reaction was freeze−pump−thawed three times, was back-filled with N_2, and was stirred overnight at room temp (60 °C for the tosyl amide dienynes). Flash chromatography with 5% EtOAc in hexanes (10% for the tosyl amides) yields the pure product.

The [4 + 2 + 2] Dimerization To Form 8-{[(2*E*,4*E*)-Hexa-2,4-dienyloxy]methyl}-6-methyl-1,3,3a,6-tetrahydrocycloocta[*c*]-furan (3). To a clean, dry 15-mL Schlenk tube, 30 mg of catalyst was added as a solution in 2 mL of CH_2Cl_2. H_2 was gently bubbled through the orange/red solution for 3 min causing it to become dark and cloudy. One-half of a milliliter of EtOAc was added, and N_2 was gently bubbled through the solution for 3 more minutes. **1** (52 mg, 0.38 mmol) was then added along with 1 mL of CH_2Cl_2. The reaction was freeze−pump−thawed three times, was back-filled with N_2, and was stirred overnight at room temp (60 °C for the tosyl amide dienynes). Flash chromatography with 5% EtOAc in hexanes yielded 40 mg (78%) of **3**. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.19−5.98 (m, 2H), 5.73−5.51 (m, 4H), 5.40 (d, J = 6.6 Hz, 1H), 5.03 (dd, J = 10.0, 5.9 Hz, 1H), 4.42 (d, J = 13.7 Hz, 1H), 4.30 (d, J = 13.7 Hz, 1H), 4.20−4.07 (m, 2H), 3.90 (d, J = 6.1 Hz, 2H), 3.85−3.73 (m, 3H), 1.07 (d, J = 6.7 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 149.1, 136.9, 136.8, 133.3, 130.9, 130.8, 129.9, 126.7, 120.8, 117.1, 76.5, 75.2, 74.0, 70.0, 42.4, 32.4, 20.2, 18.1; IR (thin film) 2852.6, 2868.0, 2914.3,2929.7, 2959.6, 2998.2, 3015.5, 2338.6, 2361.7, 1362.6, 1374.2, 1435.9, 1457.1, 1652.9, 1662.5, 1669.3, 1675.1, 1684.7, 1690.5, 1695.3, 1700.2, 1717.5, 1733.9, 668.3, 937.3, 990.3, 990.4, 1054.0, 1073.3, 110.9, 1139.9 cm^{-1}; MS-EI *m*/*z* (% relative intensity) 272 (M^+, 4), 174.1 (30), 159.1 (8), 145.1 (21), 133.1 (29), 105.1 (55), 91.7 (57), 81.1 (100), 65.1 (17), 53.1 (28), MS-HREI calculated for $C_{18}H_{24}O_2$ (M^+) *m*/*e* 272.1776, measured *m*/*e* 272.1775.

General Procedure for the [4 + 2 + 2] Cocyclization of a Dienyne and Terminal Alkyne. To a clean, dry 15-mL Schlenk tube, 30 mg of catalyst was added as a solution in 2 mL of CH_2Cl_2. H_2 was gently bubbled through the orange/red solution for 3 min causing it to become dark and cloudy. One-half of a milliliter of EtOAc was added, followed by sparging with N_2 for 3 min. The terminal alkyne (1.9 mmol) was added along with 0.5 mL of CH_2Cl_2, and the reaction was stirred to ensure homogeneity. Finally, the dienyne (0.38 mmol) was added along with 0.5 mL of CH_2Cl_2. The reaction was freeze−pump−thawed three times, was back-filled with N_2, and was stirred overnight in a 60 °C oil bath. Flash chromatography with 5% or 10% EtOAc in hexanes provided the pure product.

8-[(Benzyloxy)methyl]-6-methyl-1,3,3a,6-tetrahydrocycloocta-[*c*]furan (20). To a clean, dry 15-mL Schlenk tube, 30 mg of catalyst was added as a solution in 1 mL of CH_2Cl_2. H_2 was gently bubbled through the orange/red solution for 3 min causing it to become dark and cloudy. One-half of a milliliter of EtOAc was added, and N_2 was gently bubbled through the solution for 3 more minutes. Benzyl propargyl ether (278 mg, 1.9 mmol) was added

with 1 mL of CH_2Cl_2. **1** (47 mg, 0.38 mmol) was then added along with 1 mL of CH_2Cl_2. The reaction was freeze−pump−thawed three times, was back-filled with N_2, and was stirred overnight 60 °C. Flash chromatography with 5% EtOAc in hexanes yielded 76.3 mg (73%) of **20**. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.38−7.26 (m, 5H), 5.79 (dd, J = 2.5 Hz, 1H), 5.60 (ddd, J = 9.5, 9.5, 2.2, 1H), 5.44 (d, J = 6.6 Hz, 1H), 5.07 (ddd, J = 9.9, 5.5, 1.1 Hz, 1H), 4.47 (m, 3H), 4.31 (d, J = 13.5 Hz, 1H), 4.21 (t, J = 7.7 Hz, 1H), 4.17−4.11 (m, 1H), 3.86 (s, 2H), 3.82−3.80 (m, 1H), 3.66 (t, J = 7.7 Hz, 1H), 1.11 (d, J = 6.9 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 149.2, 138.2, 137.1, 136.9, 130.7, 128.3, 127.8, 127.5, 120.7, 117.1, 76.6, 75.2, 74.0, 71.4, 42.4, 32.4, 20.2; IR (thin film) 3305.8, 3065.7, 3030.7, 2939.6, 2856.1, 2247.2, 1952.3, 1731.7, 1640.1, 1496.3, 1454.0, 1357.7, 1357.7, 1311.7, 1249.4, 1206.2, 1161.2, 1069.0, 1028.0, 924.6, 909.1, 845.7, 733.1, 698.2, 605.6, 542.2, 464.2 cm^{-1}; MS-HREI calcd for $C_{18}H_{20}O_2Li$ (MLi^+) *m*/*e* 275.1623, measured *m*/*e* 275.1620.

General Procedure for the [4 + 2 + 2] Cocyclization of a Dienyne and Acetylene. To a clean, dry 15-mL Schlenk tube equipped with a stir bar, Rh/DuPHOS/SbF_6 (30 mg) was added as a solution in CH_2Cl_2 (2 mL). The solution was stirred at room temperature while ethyl acetate (0.5 mL) was added via syringe. The dienyne (0.38 mmol) was added as a solution in CH_2Cl_2 (1 mL), and the tube was sealed. The tube was then put through a freeze−pump−thaw cycle three times and was placed in an ice bath. Acetylene was then bubbled through the solution for 5 min and the tube was once again sealed and stirred overnight in a 60 °C oil bath. The reaction mixture was then concentrated and flash chromatography (10% ethyl acetate in hexanes) afforded the pure product.

6-Methyl-1,3,3a,6-tetrahydrocycloocta[*c*]furan (43). To a clean, dry 15-mL Schlenk tube equipped with a stir bar, Rh/DuPHOS/SbF_6 (60 mg) was added as a solution in CH_2Cl_2 (4 mL). The solution was stirred at room temperature while ethyl acetate (1 mL) was added via syringe. (2*E*,4*E*)-1-(Prop-2-ynyloxy)-hexa-2,4-diene (**1**) (51.7 mg, 0.38 mmol) was added as a solution in CH_2Cl_2 (2 mL), and the tube was sealed. The tube was then put through a freeze−pump−thaw cycle three times and was placed in an ice bath. Acetylene was bubbled through the solution for 5 min and the tube was once again sealed and stirred overnight in a 60 °C oil bath. Upon completion, the reaction mixture was concentrated and flash chromatography (10% ethyl acetate in hexanes) afforded 70.5 mg (62% yield) of 6-methyl-1,3,3a,6-tetrahydrocycloocta[*c*]furan as a yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.67 (dd, J = 7.7, 2.2 Hz, 1H), δ 5.50 (d, J = 13.4 Hz, 1H), δ 5.47 (d, J = 10.1 Hz, 1H), δ 5.32 (dd, J = 11.8 Hz, 5.7 Hz, 1H), δ 5.05 (dd, J = 9.9, 6.3 Hz, 1H), δ 4.39 (d, J = 13.4 Hz, 1H), δ 4.26 (d, J = 14.0 Hz, 1H), δ 4.23−4.16 (m, 2H), δ 3.83−3.76 (m, 1H), δ 3.69−3.61 (m, 1H), δ 1.10 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.5, 139.1, 135.3, 122.4, 120.7, 115.5, 75.2, 73.8, 41.9, 32.3, 20.4. MS-HRES calculated for $C_{11}H_{14}O$ (M^+Na) *m*/*e* 185.0942, measured *m*/*e* 185.0945.

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Supporting Information Available: Complete experimental details including procedures for the preparation of the dienyne substrates, compound characterization, and NMR spectra are available. This material is available free of charge via the Internet at http://pubs.acs.org.

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