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Ruthenium Alkylidene-Catalyzed Reaction of 1,6-Heptadiynes with Alkenes

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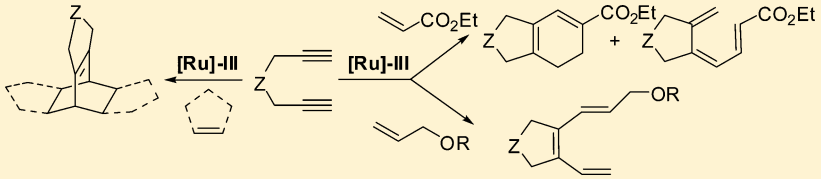
Supporting Information



ABSTRACT: Ruthenium carbene catalysts are able to catalyze cross [2 + 2 + 2] cyclotrimerizations of 1,6-diynes with cyclic and acyclic double bonds. A plausible mechanistic competition is described in which electron-deficient alkenes follow similar pathways as those of other ruthenium catalysts previously utilized and produce mixtures of trienes and cyclohexadienes. On the contrary, allylethers give different isomers of the same final products, suggesting that a metathetic cascade pathway operates in these cases.

Metal-catalyzed [2 + 2 + 2] cyclotrimerization of alkynes is a feasible approach to construct densely functionalized aromatic compounds in an atom-efficient and group-tolerant way.[1−9] Aromatic and nonaromatic heterocycles have also been obtained by cross reactions between alkynes and carbon−heteroatom multiple bonds, such as nitriles to give pyridines[10] or heterocumulenes which give access to 2-pyridones.[11,12] The participation of carbon−carbon double bonds in [2 + 2 + 2] cyclizations is possible, but this has been much less developed owing to the lack of generality. The reaction of two alkyne units with an alkene gives, in principle, substituted cyclohexadiene derivatives, which are valuable synthetic intermediates. Several metal complexes are able to mediate these kinds of transformations. Stoichiometric reactions were reported using cobalt-based systems.[13,14] Catalytic versions have been developed using rhodium,[15−17] iridium,[18] cobalt,[19,20] nickel,[21,22] and niobium complexes.[23] Catalytic enantioselective [2 + 2 + 2] cycloadditions of one alkyne unit and two alkenes were described using cobalt[24] and nickel catalysis.[25] Intramolecular reactions with dienynes catalyzed by rhodium complexes allowed the synthesis of fused polycyclic compounds.[26−28]

Ruthenium catalysts such as [Cp*RuCl(cod)] have been used for the reaction of 1,6-diynes with alkenes. The [2 + 2 + 2] cycloaddition was found to compete with double cyclopropanation processes, which showcased the double carbenic nature of the metallacyclopentadiene intermediate.[29] A recent study focused on the regio- and stereochemical outcome of the reaction, which depends on the substitution of the 1,6-diyne and the nature of the alkene. With cyclic alkenes, the expected cyclohexadiene is formed and a tandem [2 + 2 + 2]/[4 + 2] cycloaddition is also observed. When acyclic alkenes were used, a cascade process that behaves as a formal Ru(II)-catalyzed [2 + 2 + 2] cycloaddition took place. Initially, a Ru-catalyzed linear coupling occurs to give open 1,3,5-trienes, which, after a thermal disrotatory 6e$^-$ π-electrocyclization, led to the final 1,3-cyclohexadienes.[30]

The mechanism of the [2 + 2 + 2] alkyne cyclotrimerization is well-established, and its basic features have been studied mainly through computational procedures.[31] Independently, the groups of Vollhardt[32] and Saá[33] studied, by DFT computations, the mechanism of the cobalt- and ruthenium-mediated [2 + 2 + 2] cycloaddition of two alkynes to one alkene to give 1,3-cyclohexadienes, respectively.

Blechert reported for the first time the use of Grubbs' first-generation catalyst [**Ru**]-**I** for the intramolecular cyclotrimerization of triynes and he proposed a cascade metathetic mechanism.[34] We[35] and other groups[36−38] have shown that [**Ru**]-**I**, [**Ru**]-**II**, and Hoveyda−Grubbs' complex [**Ru**]-**III** can mediate [2 + 2 + 2] cyclotrimerization reactions for the synthesis of benzene rings. Recently, we used [**Ru**]-**III** for the efficient synthesis of pyridines[39] and 2-pyridones.[40] These latter cases showed a similar behavior in terms of scope and limitations as that of other Ru catalysts, suggesting a possible transformation of the carbenic initial complex into a different species able to follow a metallacyclopentadiene-based reaction pathway.

We present here a study on the behavior of ruthenium carbene catalysts in the reaction of diverse kinds of alkenes with 1,6-diynes. As a starting point, we selected diyne **1a** and ethyl acrylate to optimize the reaction conditions, the results of which are summarized in Table 1.

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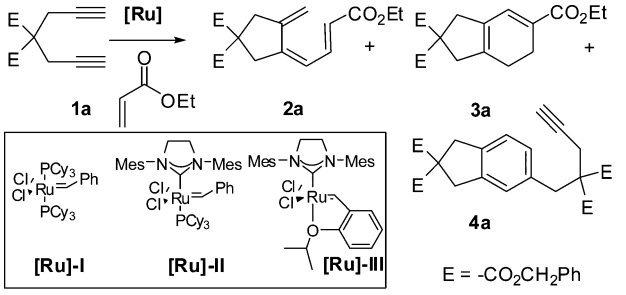
Table 1. Selection of Conditions for the Reaction of 1a with Ethyl Acrylate



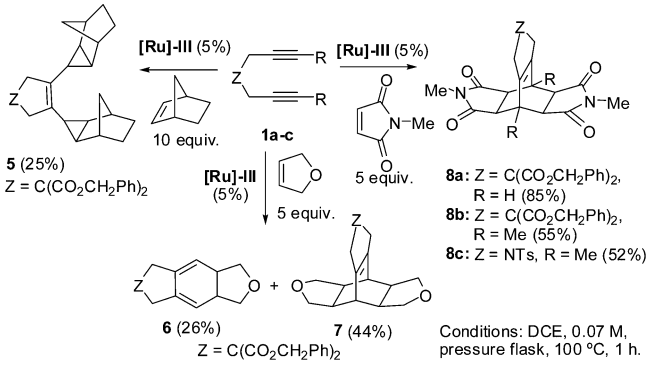
					yield (%)[a]			
entry	solvent	temp. (°C)	time (h)	cat. (mol %)	1a	2a	3a	4a
1	toluene	rt	48	5	60			16
2	toluene	110[b]	3	5		25	32	11
3	CH_3CN	82[b]	1	5	45			
4	THF	66[b]	1	5		32	13	
5	DMF	140	1	5			40	
6	DCM	40[b]	2	5	32	8	23	28
7	DCE	90[b]	2	5		12	45	35
8	DCE	90[b]	2	10		17	43	36
9	DCE	100[c]	0.5	5		45	27	16
10	DCE	100[c]	1	5		26	51	13
11	DCE	100[c]	1	10 [**Ru**]-**I**	61			
12	DCE	100[c]	1	5 [**Ru**]-**II**		21	38	15

[a]Reactions were conducted at 0.07 M diyne with 5 equiv of ethyl acrylate and catalyst [**Ru**]-**III** except for entries 11 and 12. [b]Refluxing conditions. [c]Conducted in a sealed tube.

The reactions were carried out with catalyst [**Ru**]-**III** except for entries 11 and 12 and with 5 equiv of ethyl acrylate. The initial attempts conducted in toluene showed that heating was needed to observe the cross reaction. A mixture of **2a** and **3a**, both in moderate yields, was observed under refluxing toluene (entry 2, Table 1), resulting in the isolation of small amounts of dimerization product **4a**. Other solvents were tested (entries 3−7), and with DCE the total conversion of the starting diyne into a mixture of **2a**, **3a**, and **4a** was observed. It is noteworthy that in the case of DMF at 140 °C only cyclized product **3a** was observed, albeit in moderate yield (entry 5). Very similar results were observed with 5 and 10 mol % catalyst loading (entries 7 and 8). The reaction was then performed in a sealed tube because we had observed that this method was favorable when developing the reaction of diynes with nitriles.[39] Under these conditions, the global yield improved and the ratio **3a**/**2a** increased with longer reaction times (entries 9 and 10). Next, we used the latter conditions (conditions A) with [**Ru**]-**I** and [**Ru**]-**II** as the catalysts (entries 11 and 12). First-generation catalyst gave no final products, possibly due to decomposition under the reaction conditions. Using [**Ru**]-**II** resulted in yields that were slightly below those achieved with [**Ru**]-**III**, which was used for the rest of the study.

Our next aim was to establish the scope of the process by reacting diynes **1a−c** with different cyclic alkenes (Scheme 1).[41] Norbornene reacted poorly because a great amount of norbornene polymer was formed. Compound **5** could be isolated in low yield using 10 equiv of this alkene. This type of dicyclopropane was described previously by Itoh using other diynes.[29] Reaction with dihydrofurane gave a mixture of the expected [2 + 2 + 2] product, **6**, and a Diels−Alder adduct, **7**,

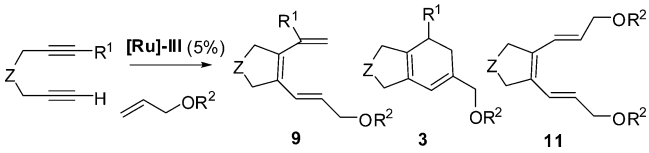
Scheme 1. Cyclotrimerization of Cyclic Alkenes with 1,6-Diynes



arising from the reaction of **6** with a second equivalent of dihydrofurane. When using methyl maleimide, the latter 2:1 adducts were the only reaction products, and the yield was good with **1a**, whereas it was moderate with diynes **1b** and **1c**.[42]

During the study on the scope of the reaction, we realized that allyl ethers produced, under our conditions, different products from those described previously.[30] In particular, reaction of **1a** with allyl phenylether produced a sluggish mixture of an open triene identified as **9b** (22%), cyclohexadiene **3b** (15%), and cycloisomer **10** (13%, entry 1, conditions A, Table 2). Product **9b** is an isomer of **2a** isolated in the reactions shown in Table 1, which indicates a possible

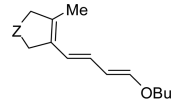
Table 2. Cyclization Reactions of 1,6-Diynes 1 with Allyl Ethers



no.	diyne	Z	R^1	R^2	cond.[a]	yield (%)
1	**1a**	$C(CO_2Bn)_2$	H	Ph	A	**9b**: 22; **3b**: 15; **10**[b]: 13
2	**1a**	$C(CO_2Bn)_2$	H	Ph	B	**9b**: 73; **11b**: 10
3	**1a**	$C(CO_2Bn)_2$	H	Bu	A	**9c**: 19; **12**[c]: 26
4	**1a**	$C(CO_2Bn)_2$	H	Bu	B	**9c**: 62; **11c**: 15
5	**1d**	NTs	H	Ph	A	**9d**: 27
6	**1d**	NTs	H	Ph	B	**9d**: 55
7	**1d**	NTs	H	Bu	B	**9e**: 45
8	**1e**	O	H	Bu	B[d]	**9f**: 38
9	**1f**	NTs	Me	Ph	A	**9g**: 16; **3g**: 32
10	**1f**	NTs	Me	Ph	B	**9g**: 61
11	**1g**	$C(CO_2Bn)_2$	Me	Ph	B	**9h**/**3h** (4:1) 45[e]

[a]Conditions A: DCE 0.07 M, 5 equiv of allyl ether, sealed tube, 100 °C, 1 h. Conditions B: $CHCl_3$ 0.07 M, 5 equiv of allyl ether, rt, 16 h. [b]**10**:

[c]**12**:



[d]Concentration: 1.1 mM. [e]A 4:1 mixture (calculated from integration of well-resolved signals) of **9g** and **3g** that could not be separated.

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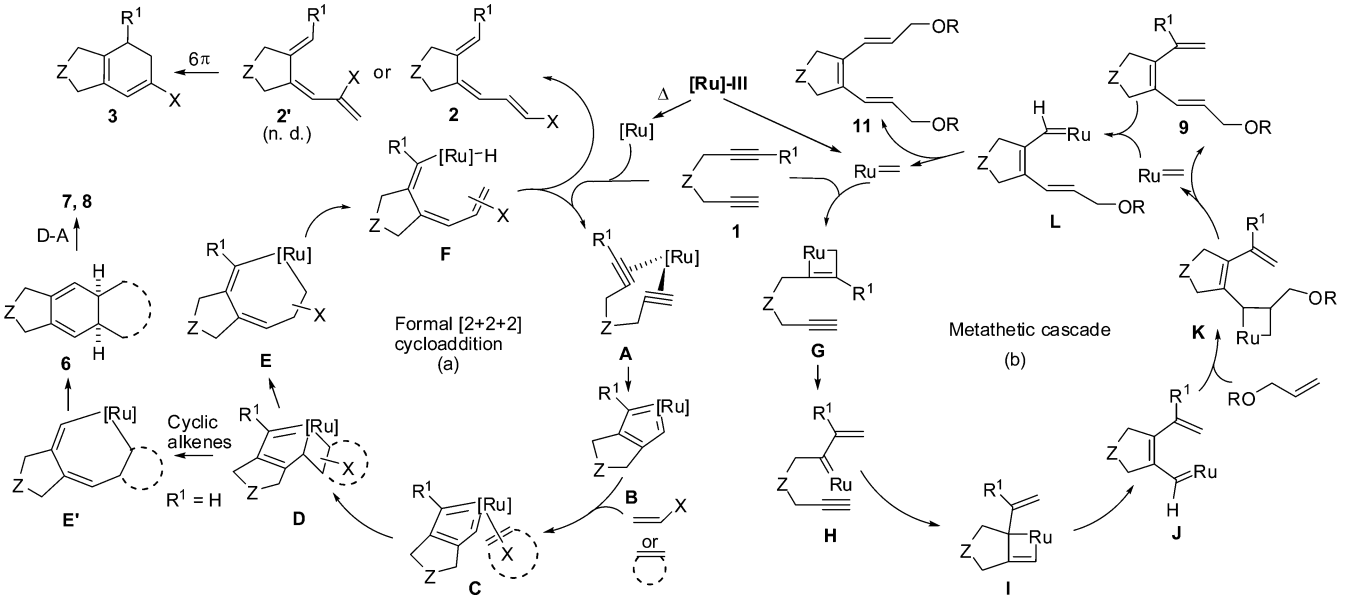
Scheme 2. Reaction Pathways for Cyclization Reactions



change in the reaction pathway. The result of this reaction was substantially improved when we carried it out at room temperature for 16 h (conditions B, entry 2). In this case, the major product was **9b** (73%), and a new product assigned to **11b** was also obtained in 10% yield. The reaction of **1a** with allyl butyl ether under conditions A gave a poor result, although, interestingly, a new product, **12**, was isolated in low yield. This compound shares the structure of **2a** (Table 1), but the conjugated olefinic system is shifted (entry 3). On the other hand, reaction under conditions B gave **9c** (62%) and **11c** (15%, entry 4). In view of this result, we selected some diynes and carried out their reaction with the allyl ethers. It was observed that conditions A gave worse results and allowed the formation of products **3** in a similar way as the reaction with ethyl acrylate (entries 1 and 9). On the contrary, milder conditions B allowed the formation of products **9** and **11** in moderate to good global yields (entries 2, 4, 6–8, 10, and 11). With unsymmetrical diynes **1f** and **1g**, the reaction was totally regioselective, with the formation of products **9g–h** and **3g** and no detection of other possible regioisomers (entries 9–11).

Our results show that ruthenium carbenes such as [**Ru**]-**III** are able to catalyze cyclizations of 1,6-diynes with different alkenes. However, it appears that two reaction pathways may be operating in these reactions. A first possible mechanism consists of a transformation of the ruthenium complex under strong reaction conditions (conditions A) into a different species, which could catalyze the cycloaddition in a similar way as that with other ruthenium catalysts (Scheme 2, path a). This pathway explains the formation of compounds **2**, which may evolve into **3** through a 6π-electrocyclization that completes a formal [2 + 2 + 2] cyclotrimerization. Transformation of ruthenium carbenes into other species able to catalyze nonmetathetic transformations has been described by us[43] and others.[44] In particular, we showed a case in which the modified species was unable to catalyze metathesis reactions.[43] After coordination with the metal to give **C**,[46] the unsymmetrical olefin inserts in the C–Ru bond with both orientations (**D**), but it does so with substituent X preferably being away from the bulky metal complex. After rearrangement of **D** into **E**, a mixture of **2** and **2′** (major) is formed from **F**. However, **2′** was not detected, as it undergoes an electrocyclization to give **3**. In a previous work by Saá, the parent compound to **2**, obtained when reacting a nonterminal diyne with an allyl ether, could be isolated only when the reaction was performed at room temperature, as it underwent electrocyclization at 50 °C with no catalyst needed.[30] In our case, it was observed that the isomer **2** did not cyclize and could be isolated, whereas its isomer, **2′**, was not detected. In the case of cyclic alkenes, direct [2 + 2 + 2] cycloaddition from **D** leads to **E′**, which gives products like **6** that can further undergo a Diels–Alder cycloaddition onto **7** or **8** (Scheme 1). On the other hand, with allyl ethers, although this pathway still operates if the same strong conditions are applied, a metathetic cascade process would be possible if the ruthenium species is not transformed and allowed to react for a longer period. Thus, following cycle b in Scheme 2, successive metatheses produce intermediates **H** and **J**. This latter carbene reacts with allyl ether to give **9**, which might continue reacting with the catalysts and the excess alkene to produce **11** through intermediate **L**. Neither **9** nor **11** give cyclized products. Previous reports have shown the need for harsh thermal conditions or photochemical mediation to produce 6π-cyclizations with these products.[45] Interestingly, when using unsymmetrically substituted diynes **1g–h**, the reactions behave in a completely regioselective manner. Thus, no other isomers could be detected, which is possibly due to steric reasons in the coordination step of the alkene (from **B** to **C**). The selectivity in the metathesis pathway may be due to equilibration from reaction intermediates, as it has been shown that the metal has higher affinity for terminal alkynes.[47] However, the formation of intermediate **K** would possibly be sterically precluded if R^1 is attached to the ruthenacyclobutane and equilibration possibly leads to the observed isomer.

To obtain more information on these processes, we monitorized some of the reactions by ^{1}H NMR, observing the evolution of the carbenic signal (see the Supporting Information). Thus, the reaction of **1a** with ethyl acrylate in the presence of 25 mol % of [**Ru**]-**III** at 100 °C showed the rapid disappearance of the carbenic signal (16.390 ppm), suggesting the transformation of the catalyst. If the same reaction is carried out at rt, then the carbene remains unaltered and no reaction is

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observed. In the reaction of **1a** with allyl phenyl ether at rt, a new carbenic signal appears during the reaction (15.807 ppm). This new carbene could correspond to **J** in Scheme 2.[48] No other intermediates containing carbenic hydrogens appear in the proposed reaction pathways.

In conclusion, we have shown a new nonmetathetic application of ruthenium carbenes as catalysts for cross diyne−alkene cyclizations. Different cyclization products are isolated depending on the reaction conditions and the nature of the alkene, suggesting a competition between two reaction pathways.

EXPERIMENTAL SECTION

Reaction of Diyne 1a with Ethyl Acrylate. (Table 1, entry 10, conditions A.) A solution of **Ru**-[**III**] (9 mg, 0.014 mmol) in 1,2-dichloroethane (2 mL) was added to a solution of the diyne **1a** (100 mg, 0.28 mmol) and the ethyl acrylate (140 mg, 0.15 mL, 1.40 mmol) in the same solvent (2 mL) contained in a pressure flask. The flask was sealed, introduced in a 100 °C bath and the resulting mixture was stirred during 1 h. After cooling the flask to room temperature the reaction mixture was filtered through Celite, the solvent was eliminated under reduced pressure and the residue was purified by silica-gel flash column chromatography with solvent mixtures (EtOAc/hexanes 1:9 v/v). Evaporation of solvent afforded 34 mg (26%) of **2a**, 66 mg (51%) of **3a** and 26 mg (13%) of **4a**. If the reaction time was shortened to 30 min (Table 1, entry 9) the reaction gave 58 mg (45%) of **2a**, 35 mg (27%) of **3a**, and 32 mg (16%) of **4a**.[29]

(*Z*)-Dibenzyl 3-((*E*)-4-Ethoxy-4-oxobut-2-enylidene)-4-methylenecyclopentane-1,1-dicarboxylate, 2a. Yellow oil. R_f 0.21 (EtOAc/hexanes 1:6). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (t, 3H, J = 7.2 Hz), 3.09 (s, 2H), 3.20 (s, 2H), 4.19 (q, 2H, J = 7.2 Hz), 5.12 (s, 4H), 5.17 (d, 1H, J = 10.5 Hz), 5.28 (s, 1H), 5.34 (s, 1H), 5.67 (d, 1H, J = 10.9 Hz), 7.10 (t, 1H, J = 11.6 Hz), 7.22−7.24 (m, 4H), 7.29−7.31 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 14.3, 42.0, 42.4, 57.2, 60.0, 67.4, 115.0, 118.0, 121.7, 128.0, 128.3, 128.5, 135.3, 139.8, 143.5, 145.8, 166.6, 170.7; IR (NaCl): 2924, 2852, 1736, 1637 cm^{-1}; Anal. Calcd for $C_{28}H_{28}O_6$: C, 73.03; H, 6.13. Found: C, 73.14; H, 6.32.

2,2-Dibenzyl 5-Ethyl 6,7-dihydro-1*H*-indene-2,2,5(3*H*)-tricarboxylate, 3a. Colorless oil. R_f 0.15 (EtOAc/hexanes 1:6). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (t, 3H, J = 7.1 Hz), 2.24 (t, 2H, J = 9.9 Hz), 2.54 (t, 2H, J = 9.9 Hz), 3.11 (bs, 4H), 4.19 (q, 2H, J = 7.1 Hz), 5.12 (s, 4H), 6.94 (s, 1H), 7.22−7.26 (m, 4H), 7.30−7.32 (m, 6H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 14.4, 22.1, 23.5, 40.9, 43.4, 58.8, 60.4, 67.4, 126.9, 128.1, 128.4, 128.6, 130.4, 131.4, 135.4, 140.9, 167.3, 171.5; IR (NaCl): 2966, 2928, 1740 cm^{-1}; Anal. Calcd for $C_{28}H_{28}O_6$: C, 73.03; H, 6.13. Found: C, 73.15; H, 6.21.

Compound 5. A solution of **Ru**-[**III**] (9 mg, 0.014 mmol) in 1,2-dichloroethane (2 mL) was added to a solution of diyne **1a** (100 mg, 0.28 mmol) and norbornene (263 mg, 2.80 mmol) in the same solvent (2 mL) contained in a pressure flask. The flask was sealed and introduced in a 100 °C bath, and the resulting mixture was stirred during 16 h. After cooling the flask to room temperature, the reaction mixture was filtered through Celite, the solvent was eliminated under reduced pressure, and the residue was purified by silica-gel flash column chromatography with solvent mixtures (EtOAc/hexanes 1:20 → 1:6 v/v). Evaporation of solvent afforded 38 mg (25%) of **5**.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.65 (d, 2H, J = 10.6 Hz), 0.87 (d, 4H, J = 2.5 Hz), 1.05 (d, 2H, J = 10.5 Hz), 1.22−1.25 (m, 4H), 1.43−1.45 (m, 4H), 1.61 (t, 2H, J = 2.8 Hz), 2.29 (s, 4H), 2.70 (s, 4H), 5.08 (s, 4H), 7.21−7.23 (m, 4H), 7.29−7.31 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 12.8, 22.0, 28.2, 29.5, 36.0, 41.1, 57.5, 67.1, 128.0, 128.2, 128.5, 131.4, 135.6, 171.7; IR (NaCl): 2961, 2921, 2849, 1735, 1577 cm^{-1}; Anal. Calcd for $C_{37}H_{40}O_4$: C, 80.99; H, 7.35. Found: C, 81.15; H, 7.21.

General Procedure for the Reaction of Diynes with Cyclic Alkenes. A solution of **Ru**-[**III**] (9 mg, 0.014 mmol) in 1,2-dichloroethane (2 mL) was added to a solution of the diyne and the cyclic alkene in the same solvent (2 mL) contained in a pressure flask. The flask was sealed and introduced in a 100 °C bath, and the resulting mixture was stirred during 1 h. After cooling the flask to room temperature, the reaction mixture was filtered through Celite, the solvent was eliminated under reduced pressure, and the residue was purified by silica-gel flash column chromatography with solvent mixtures (EtOAc/hexanes 1:20 → 1:1 v/v).

Dibenzyl 3,3a,7,8a-Tetrahydro-1*H*-indeno[5,6-*c*]furan-6,6-(5*H*)dicarboxylate, 6. Following general procedure the reaction of cyclic alkenes, diyne **1a** (100 mg, 0.28 mmol) and 2,5-dihydrofuran (98 mg, 1.40 mmol) afforded 31 mg (26%) of **6** as a light yellow syrup (R_f 0.08 (EtOAc/hexanes 1:6)) and 62 mg (44%) of **7** as a yellow syrup (R_f 0.07 (EtOAc/hexanes 1:6)). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.92−3.05 (m, 6H), 3.45 (dd, 2H, J_1 = 8.1 Hz, J_2 = 6.2 Hz), 4.12 (t, 2H, J = 7.8 Hz), 5.12 (s, 2H), 5.13 (s, 2H), 5.41 (s, 2H), 7.23−7.24 (m, 4H), 7.30−7.31 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 38.68, 38.74, 58.9, 67.2, 75.2, 117.4, 127.9, 128.0, 128.3, 128.50, 128.52, 134.7, 135.41, 135.44, 170.9, 171.0; IR (NaCl): 2960, 2928, 2857, 1736, 1552 cm^{-1}; Anal. Calcd for $C_{27}H_{26}O_5$: C, 75.33; H, 6.09. Found: C, 75.58; H, 6.12.

Compound 7. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.63−1.65 (m, 2H), 1.71−1.72 (m, 4H), 2.76 (s, 4H), 3.71 (d, 4H, J = 8.2 Hz), 3.88 (d, 4H, J = 8.4 Hz), 5.10 (s, 4H), 7.21−7.24 (m, 4H), 7.30−7.32 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 19.2, 23.4, 41.0, 57.3, 67.3, 69.7, 128.0, 128.3, 128.5, 130.4, 135.4, 171.5; IR (NaCl): 2964, 2924, 2852, 1736, 1547 cm^{-1}; Anal. Calcd for $C_{31}H_{32}O_6$: C, 74.38; H, 6.44. Found: C, 74.25; H, 6.31.

Compound 8a. Following general procedure the reaction of cyclic alkenes, diyne **1a** (100 mg, 0.28 mmol) and *N*-methylmaleimide (155 mg, 1.40 mmol) afforded 139 mg (85%) of **8a** as a yellow syrup (R_f 0.11 (EtOAc/hexanes 1:3)). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.76 (s, 6H), 2.88 (s, 4H), 3.00 (s, 4H), 3.81 (s, 2H), 5.02 (s, 4H), 7.15−7.18 (m, 4H), 7.29−7.31 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 24.7, 35.1, 42.1, 43.5, 58.6, 67.4, 127.9, 128.4, 128.6, 135.1, 136.7, 170.7, 176.3; IR (NaCl): 2924, 1732, 1700 cm^{-1}; Anal. Calcd for $C_{33}H_{30}N_2O_8$: C, 68.03; H, 5.19, N, 4.81. Found: C, 68.25; H, 5.01, N, 4.72.

Compound 8b. Following general procedure the reaction of cyclic alkenes, diyne **1b** (100 mg, 0.26 mmol) and *N*-methylmaleimide (144 mg, 1.30 mmol) afforded 87 mg (55%) of **8b** as a yellow syrup (R_f 0.07 (EtOAc/hexanes 1:3)). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.91 (s, 6H), 2.67 (s, 4H), 2.77 (s, 6H), 2.89 (s, 4H), 5.02 (s, 4H), 7.15−7.18 (m, 4H), 7.29−7.31 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 17.3, 24.7, 40.6, 41.2, 50.0, 58.3, 67.5, 128.0, 128.4, 128.6, 135.1, 138.3, 170.8, 175.1; IR (NaCl): 2924, 1732, 1700 cm^{-1}; Anal. Calcd for $C_{35}H_{34}N_2O_8$: C, 68.84; H, 5.61; N, 4.59. Found: C, 68.80; H, 5.58, N, 4.61.

Compound 8c. Following general procedure the reaction of cyclic alkenes, diyne **1c** (75 mg, 0.27 mmol) and *N*-methylmaleimide (151 mg, 1.36 mmol) afforded 70 mg (52%) of **8c** as a yellow syrup (R_f 0.05 (EtOAc/hexanes 1:3)).^{1}H NMR (400 MHz, $CDCl_3$): δ 1.86 (s, 6H), 2.41 (s, 3H), 2.59 (s, 6H), 2.68 (s, 4H), 3.96 (s, 4H), 7.35 (d, 2H, J = 8.2 Hz), 7.64 (d, 2H, J = 8.2 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.8, 21.4, 24.6, 40.5, 49.9, 54.4, 127.5, 129.9, 133.3, 136.5, 143.7, 174.5 ppm; IR (NaCl): 2916, 2853, 1710, 1551 cm^{-1}; Anal. Calcd for $C_{25}H_{27}N_3O_6S$: C, 60.35; H, 5.47; N, 8.45; S, 6.44. Found: C, 60.41; H, 5.38, N, 8.51.

General Procedure for the Reaction of Diynes with Allyl Ethers. Conditions A, Table 2. A solution of **Ru**-[**III**] (9 mg, 0.014 mmol) in 1,2-dichloroethane (2 mL) was added to a solution of the diyne (0.28 mmol) and the allyl ether (1.40 mmol) in the same solvent (2 mL) contained in a pressure flask. The flask was sealed and introduced in a 100 °C bath, and the resulting mixture was stirred during 1 h. After cooling, it was filtered through Celite. The solvent was eliminated under reduced pressure, and the residue was purified by silica-gel flash column chromatography with solvent mixtures (EtOAc/hexanes 1:20 → 1:6 v/v).

Conditions B, Table 2. A solution of **Ru**-[**III**] (9 mg, 0.014 mmol) in $CHCl_3$ (2 mL) was added to a solution of the diyne (0.28 mmol) and the allyl ether (1.40 mmol) in the same solvent (2 mL).

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The mixture was stirred for 16 h, and the same work up as that under the previous conditions was followed.

Reaction of 1a with Allyl Phenyl Ether. Following conditions A, diyne **1a** (100 mg) and allyl phenyl ether (188 mg) afforded 30 mg (22%) of **9b** as a yellow oil (R_f 0.16 (EtOAc/hexanes 1:6)), 21 mg (15%) of **3b** as a colorless oil (R_f 0.17 (EtOAc/hexanes 1:6) impurified with **9b**), and 24 mg (13%) of **10** as a yellow oil (R_f 0.51 (EtOAc/hexanes 1:6)). Following conditions B, 101 mg (73%) of **9b** and 17 mg (10%) of **11b** as a colorless syrup (R_f 0.36 (EtOAc/hexanes 1:6)).

(*E*)-Dibenzyl 3-(3-Phenoxyprop-1-enyl)-4-vinylcyclopent-3-ene-1,1-dicarboxylate, 9b. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.29 (s, 2H), 3.31 (s, 2H), 4.61 (d, 2H, J = 5.6 Hz), 5.12 (s, 4H), 5.18 (d, 1H, J = 17.7 Hz), 5.19 (d, 1H, J = 10.1 Hz), 5.85 (dt, 1H, J_1 = 15.7 Hz, J_2 = 5.6 Hz), 6.72−6.82 (m, 2H), 6.90−6.97 (m, 3H), 7.22−7.30 (m, 12H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ δ40.9, 41.3, 57.0, 67.4, 68.5, 114.7, 116.3, 120.9, 125.4, 126.7, 128.0, 128.3, 128.5, 129.1, 129.5, 134.0, 135.4, 135.9, 158.5, 171.5; IR (NaCl): 2930, 2853, 1733, 1546 cm^{-1}; Anal. Calcd for $C_{32}H_{30}O_5$: C, 77.71; H, 6.11. Found: C, 77.57; H, 6.25.

Dibenzyl 6-(Phenoxymethyl)-4,5-dihydro-1*H*-indene-2,2(3*H*)-dicarboxylate, 3b. Data Obtained from a Mixture of 3b and 9b. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.20−2.25 (m, 2H), 2.31−2.36 (m, 2H), 3.06 (bs, 4H), 4.47 (s, 2H), 5.11 (s, 4H), 5.93 (s, 1H), 6.90−6.97 (m, 3H), 7.23−7.31 (m, 12H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 23.2, 24.7, 41.3, 43.2, 58.7, 67.2, 71.1, 114.8, 119.8, 120.8, 128.0, 128.2, 128.5, 129.4, 129.9, 132.4, 133.5, 135.5, 158.8, 171.8.

Dibenzyl 3,4-Bis((*E*)-3-phenoxyprop-1-enyl)cyclopent-3-ene-1,1-dicarboxylate, 11b. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.31 (s, 4H), 4.63 (d, 4H,J = 5.5 Hz), 5.12 (s, 4H), 5.87 (dt, 2H, J_1 = 15.7 Hz, J_2 = 5.7 Hz), 6.79 (d, 2H, J = 15.7 Hz), 6.90−6.97 (m, 6H), 7.22−7.31 (m, 14H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 41.3, 57.1, 67.5, 68.5, 114.7, 121.0, 125.3, 127.0, 128.1, 128.3, 128.6, 129.5, 134.6, 135.3, 158.5, 171.4; IR (NaCl): 2931, 2852, 1735, 1620 cm^{-1}; Anal. Calcd for $C_{39}H_{36}O_6$: C, 77.98; H, 6.04. Found: C, 77.89; H, 6.19.

Dibenzyl 3,4-Divinylcyclopent-3-ene-1,1-dicarboxylate, 10. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.28 (s, 4H), 5.13 (s, 4H), 5.16 (d, 2H, J = 17.1 Hz), 5.18 (d, 2H, J = 11.0 Hz), 6.76 (dd, 2H, J_1 = 17.1 Hz, J_2 = 11.0 Hz), 7.23−7.25 (m, 4H), 7.30−7.32 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 40.9, 56.9, 67.4, 116.0, 128.0, 128.3, 128.5, 129.2, 135.3, 135.4, 171.6; IR (NaCl): 2930, 2853, 1733, 1546 cm^{-1}; Anal. Calcd for $C_{25}H_{24}O_4$: C, 77.30; H, 6.23. Found: C, 77.14; H, 6.12.

Reaction of 1a with Allyl Butyl Ether. Following conditions A, diyne **1a** (100 mg) and allyl butyl ether (160 mg) afforded 25 mg (19%) of **9c** as a yellow oil (R_f 0.15 (EtOAc/hexanes 1:6)) and 35 mg (26%) of **12** as a colorless oil (R_f 0.14 (EtOAc/hexanes 1:6)). Following conditions B, 82 mg (62%) of **9c** and 24 mg (15%) of **11c** were afforded as colorless syrups (R_f 0.19 (EtOAc/hexanes 1:6)).

(*E*)-Dibenzyl 3-(3-Butoxyprop-1-enyl)-4-vinylcyclopent-3-ene-1,1-dicarboxylate, 9c. ^{1}H NMR (400 MHz, $CDCl_3$) 0.92 (t, 3H, J = 7.4 Hz), 1.33−1.43 (m, 2H), 1.54−1.61 (m, 2H), 3.27 (s, 2H,), 3.28 (s, 2H), 3.43 (t, 2H, J = 6.6 Hz,), 4.05 (d, 2H, J = 5.9 Hz), 5.12 (s, 4H), 5.16 (d, 1H, J = 18.3 Hz), 5.17 (d, 1H, J = 9.7 Hz), 5.73 (dt, 1H, J_1 = 15.6 Hz, J_2 = 6.0 Hz), 6.65 (d, 1H, J = 15.7 Hz), 6.76 (dd, 1H, J_1 = 17.1 Hz, J_2 = 11.0 Hz), 7.22−7.24 (m, 4H), 7.30−7.31 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 13.9, 19.4, 31.9, 40.8, 41.4, 57.0, 67.4, 70.4, 71.3, 115.8, 124.5, 128.0, 128.3, 128.5, 128.8, 129.2, 134.4, 135.1, 135.4, 171.5; IR (NaCl): 3034, 2972, 2960, 2853, 1736, 1618 cm^{-1}. Anal. Calcd for $C_{30}H_{34}O_5$: C, 75.92; H, 7.22. Found: C, 75.78; H, 7.39.

Dibenzyl 3-((1*E*, 3*E*)-4-Butoxybuta-1,3-dienyl)-4-methylcyclopent-3-ene-1,1-dicarboxylate, 12. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.93 (t, 3H, J = 7.4 Hz), 1.37−1.43 (m, 2H), 1.55 (s, 3H), 1.63−1.65 (m, 2H), 2.97 (s, 2H), 3.01 (s, 2H), 3.68 (t, 2H, J = 6.5 Hz), 5.11 (s, 4H), 5.31−5.34 (m, 1H), 5.37 (t, 1H, J = 12.2 Hz), 5.76 (d, 1H, J = 11.2 Hz), 6.52 (d, 1H, J = 10.5 Hz), 7.22−7.25 (m, 4H), 7.29−7.31 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 13.8, 17.5, 19.1, 31.2, 41.5, 41.7, 56.4, 67.1, 69.3, 106.0, 119.8, 120.8, 128.0, 128.2, 128.5, 131.3, 135.6, 136.4, 150.5, 171.5; IR (NaCl): 2964, 2932, 1734, 1622 cm^{-1}; Anal. Calcd for $C_{30}H_{34}O_5$: C, 75.92; H, 7.22. Found: C, 75.84; H, 7.09.

Dibenzyl 3,4-Bis((*E*)-3-butoxyprop-1-enyl)cyclopent-3-ene-1,1-dicarboxylate, 11c. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (t, 6H, J = 7.4 Hz), 1.34−1.41 (m, 4H), 1.54−1.59 (m, 4H), 3.27 (s, 4H), 3.43 (t, 4H, J = 6.6 Hz), 4.05 (d, 4H, J = 5.9 Hz), 5.12 (s, 4H), 5.72 (dt, 2H, J_1 = 15.6 Hz, J_2 = 5.9 Hz), 6.65 (d, 2H, J = 15.7 Hz), 7.23−7.31 (m, 10H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 14.0, 19.4, 31.9, 41.3, 57.1, 67.4, 70.3, 71.4, 124.6, 128.0, 128.3, 128.5, 128.6, 134.1, 135.4, 171.5; IR (NaCl): 2920, 2847, 1736, 1583 cm^{-1}; Anal. Calcd for $C_{35}H_{44}O_6$: C, 74.97; H, 7.91. Found: C, 74.87; H, 7.82.

Reaction of 1d with Allyl Phenyl Ether. Following conditions B, diyne **1d** (70 mg) and allyl phenyl ether (188 mg) afforded 59 mg (55%) of **9d** as a yellow oil (R_f 0.12 (EtOAc/hexanes 1:6)).

(*E*)-3-(3-Phenoxyprop-1-en-1-yl)-1-tosyl-4-vinyl-2,5-dihydro-1*H*-pyrrole, 9d. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.43 (s, 3H), 4.31 (s, 4H), 4.60 (dd, 2H, J_1 = 5.4 Hz, J_2 = 1.1 Hz), 5.09 (d, 1H, J = 17.4 Hz), 5.24 (d, 1H, J = 10.8 Hz), 5.75 (dt, 1H, J_1 = 15.9 Hz, J_2 = 5.5 Hz), 6.63 (dd, 1H, J_1 = 17.4 Hz, J_2 = 10.8 Hz), 6.67 (d, 1H, J = 15.9 Hz), 6.90 (dd, 2H, J_1 = 8.8 Hz, J_2 = 1.0 Hz), 6.96 (t, 1H, J = 7.4 Hz), 7.29 (dd, 2H, J_1 = 8.8 Hz, J_2 = 7.4 Hz), 7.32 (d, 2H, J = 8.0 Hz), 7.75 (d, 2H, J = 8.2 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 21.5, 55.0, 55.2, 68.0, 114.7, 117.4, 121.1, 122.7, 126.9, 127.5, 127.9, 129.6, 129.9, 131.3, 132.8, 133.8, 143.7, 158.3; IR (NaCl): 2925, 2853, 1587 cm^{-1}; Anal. Calcd for $C_{22}H_{23}NO_3S$: C, 69.26; H, 6.08; N, 3.67; S, 8.41. Found: C, 69.02; H, 6.16; N, 3.75

Reaction of 1d with Allyl Butyl Ether. Following conditions B, diyne **1d** (70 mg) and allyl butyl ether (160 mg) afforded 46 mg (45%) of **9e** as a yellow oil (R_f 0.11 (EtOAc/hexanes 1:6)).

(*E*)-3-(3-Butoxyprop-1-en-1-yl)-1-tosyl-4-vinyl-2,5-dihydro-1*H*-pyrrole, 9e. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (t, 3H, J = 7.4 Hz), 1.33−1.42 (m, 2H), 1.53−1.60 (m, 2H), 2.43 (s, 3H), 3.43 (t, 2H, J = 7.8 Hz), 4.03 (dd, 2H, J_1 = 5.7 Hz, J_2 = 1.0 Hz), 4.29 (s, 4H), 5.06 (d, 1H, J = 17.4 Hz), 5.22 (d, 1H, J = 17.4 Hz), 5.63 (dt, 1H, J_1 = 15.8 Hz, J_2 = 5.7 Hz), 6.54 (d, 1H, J = 15.8 Hz), 6.63 (dd, 1H, J_1 = 17.4 Hz, J_2 = 10.9 Hz), 7.32 (d, 2H, J = 8.0 Hz), 7.74 (d, 2H, J = 8.2 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 13.9, 19.3, 21.5, 31.8, 55.0, 55.3, 70.6, 70.9, 116.9, 121.8, 127.0, 127.5, 129.9, 130.0, 131.6, 132.0,133.8, 143.6; IR (NaCl): 2925, 2850 cm^{-1}; Anal. Calcd for $C_{20}H_{27}NO_3S$: C, 66.45; H, 7.53; N, 3.87; S, 8.87. Found: C, 66.22; H, 7.69; N, 3.64.

Reaction of 1e with Allyl Butyl Ether. A solution of **Ru-[III]** (9 mg, 0.014 mmol) in $CHCl_3$ (10 mL) was added to a solution of diyne **1e** (100 mg, 1.06 mmol) and allyl butyl ether (604 mg, 5.30 mmol) in the same solvent (10 mL). The mixture was stirred for 16 h, cooled, and filtered through Celite. The solvent was eliminated under reduced pressure, and the residue was purified by silica-gel flash column chromatography with solvent mixtures (EtOAc/hexanes 1:20 → 1:6 v/v). Evaporation of solvent afforded 84 mg (38%) of **9f** as a yellow oil (R_f 0.11 (EtOAc/hexanes 1:6)).

(*E*)-3-(3-Butoxyprop-1-enyl)-4-vinyl-2,5-dihydrofuran, 9f. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.93 (t, 3H, J = 7.4 Hz), 1.34−1.42 (m, 2H), 1.55−1.61 (m, 2H), 3.45 (t, 2H, J = 6.6 Hz), 4.06 (dd, 2H, J_1 = 5.8 Hz, J_2 = 1.2 Hz), 4.85 (s, 4H), 5.02 (d, 1H, J = 17.4 Hz), 5.23 (d, 1H, J = 10.8 Hz), 5.59 (dt, 1H, J_1 = 15.9 Hz, J_2 = 5.8 Hz), 6.62 (d, 1H, J = 15.9 Hz), 6.72 (dd, 1H, J_1 = 17.5 Hz, J_2 = 10.8 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 12.9, 18.3, 30.8, 69.5, 70.2, 75.0, 75.3, 115.3, 120.7, 125.7, 128.3, 132.1, 132.7; IR (NaCl): 2960, 2929, 2852 cm^{-1}; Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.89; H, 9.79

Reaction of 1f with Allyl Phenyl Ether. Following conditions A, diyne **1f** (73 mg) and allyl phenyl ether (188 mg) afforded 18 mg (16%) of **9g** as a yellow oil (R_f 0.15 (EtOAc/hexanes 1:6) and 35 mg (32%) of **3g** as a yellow oil (R_f 0.13 (EtOAc/hexanes 1:6)). Following conditions B afforded 67 mg (61%) of **9g**.

(*E*)-3-(3-Phenoxyprop-1-en-1-yl)-4-(prop-1-en-2-yl)-1-tosyl-2,5-dihydro-1*H*-pyrrole, 9g. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.86 (s, 3H), 2.43 (s, 3H), 4.27 (d, 2H, J = 3.8 Hz), 4.30 (d, 2H, J = 3.8 Hz), 4.58 (d, 2H, J = 5.4 Hz), 4.86 (s, 1H), 5.07 (s, 1H), 5.73 (dt, 1H, J_1 = 16.0 Hz, J_2 = 5.5 Hz), 6.72 (d, 1H, J = 16.0 Hz), 6.88 (dd, 2H, J_1 =

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8.8 Hz, J_2 = 1.0 Hz), 6.95 (t, 1H, J = 7.4 Hz), 7.27 (t, 2H, J = 7.3 Hz), 7.33 (d, 2H, J = 8.2 Hz), 7.74 (d, 2H, J = 8.2 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 21.5, 22.4, 55.6, 57.2, 68.1, 114.7, 117.8, 121.1, 125.1, 127.51, 127.53, 129.4, 129.5, 129.9, 133.9, 135.8, 137.2, 143.6, 158.3; IR (NaCl): 2921, 2857, 1592 cm^{-1}; Anal. Calcd for $C_{23}H_{25}NO_3S$: C, 69.84; H, 6.37; N, 3.54; S, 8.11. Found: C, 70.05; H, 6.26; N, 3.61

4-Methyl-6-(phenoxymethyl)-2-tosyl-2,3,4,5-tetrahydro-1*H*-isoindole, 3g. ^1H NMR (400 MHz, $CDCl_3$): δ 0.98 (d, 3H, J = 6.8 Hz), 2.01 (dd, 1H, J_1 = 16.1 Hz, J_2 = 10.1 Hz), 2.37−2.43 (m, 2H), 2.43 (s, 3H), 4.01−4.24 (m, 4H), 4.47 (s, 2H), 5.87 (s, 1H), 6.88 (dd, 2H, J_1 = 8.8 Hz, J_2 = 1.0 Hz), 6.92−6.96 (m, 1H, J = 7.4 Hz), 7.26 (dd, 2H, J_1 = 8.7 Hz, J_2 = 7.4 Hz), 7.32 (d, 2H, J = 8.0 Hz), 7.72 (d, 2H, J = 8.2 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 18.1, 21.5, 27.6, 33.2, 55.0, 55.1, 70.6, 114.8, 116.4, 121.0, 127.4, 127.7, 129.5, 129.8, 134.2, 134.4, 135.1, 143.4, 158.6; IR (NaCl): 2962, 2921, 2853, 1546 cm^{-1}; Anal. Calcd for $C_{23}H_{25}NO_3S$: C, 69.84; H, 6.37; N, 3.54; S, 8.11. Found: C, 70.11; H, 6.30; N, 3.78

Reaction of 1g with Allyl Phenyl Ether. Following conditions B, diyne **1g** (105 mg) and allyl phenyl ether (188 mg) afforded 64 mg (45%) of a 4:1 mixture (calculated from integration of well-resolved signals) of **9h** and **3h** as a yellow oil that could not be separated (R_f 0.16 (EtOAc/hexanes 1:6)).

Data Obtained from the Mixture: (*E*)-Dibenzyl 3-(3-phenoxyprop-1-en-1-yl)-4-(prop-1-en-2-yl)cyclopent-3-ene-1,1-dicarboxylate, 9h. ^1H NMR (400 MHz, $CDCl_3$): δ 1.86 (s, 3H), 3.25 (s, 2H), 3.28 (s, 2H), 4.58 (d, 2H, J = 5.8 Hz), 4.87 (s, 1H), 5.04 (d, 1H, J = 1.8 Hz), 5.12 (s, 4H), 5.82 (dt, 1H, J_1 = 15.8 Hz, J_2 = 6.0 Hz), 6.79 (d, 1H, J = 15.9 Hz), 6.89−6.96 (m, 3H), 7.22−7.31 (m, 12H).

Dibenzyl 4-Methyl-6-(phenoxymethyl)-4,5-dihydro-1*H*-indene-2,2(3*H*)-dicarboxylate, 3h. ^1H NMR (400 MHz, $CDCl_3$): δ 0.98 (d, 3H, J = 6.8 Hz), 1.68−1.72 (m, 1H), 2.00−2.04 (m, 1H), 2.38−2.44 (m, 2H), 2.97−3.17 (m, 4H), 4.49 (s, 2H), 5.12 (s, 4H), 5.92 (s, 1H), 6.89−6.96 (m, 3H), 7.22−7.31 (m, 12H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 18.1, 22.3, 29.1, 33.4, 41.31, 41.37, 41.4, 43.8, 57.1, 58.7, 67.2, 67.4, 68.7, 71.1, 114.7, 114.8, 114.9, 116.5, 119.5, 120.79, 120.83, 126.0, 127.95, 127.97, 127.99, 128.00, 128.01, 128.03, 128.26, 128.30, 128.5, 128.6, 129.3, 129.4, 129.5, 131.6, 133.43, 135.41, 135.51, 135.53, 137.3, 139.7, 158.6, 158.8, 171.5, 171.8.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^1H and ^{13}C NMR spectra for new compounds. Figure S1: Evolution of carbenic signals for the reaction of **1a** with ethyl acrylate or allyl phenyl ether. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(41) Substrates bearing a Thorpe−Ingold effect were used because we observed better behavior of these diynes in [2 + 2 + 2] cycloadditions with alkynes; see ref 35.
(42) The [2 + 2 + 2]/[4 + 2] adducts were still the major product (**7**) or the only reaction product (**8a−c**) when using 2 equiv of alkene, but the yields were much lower (25−50%). Compounds **7** and **8** were isolated as single isomers assigned to structures **6**, **7**, and **8a−c** following previous work describing similar structures; see ref 29.
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(47) Intermediates **B** and **C** were proposed previously for reactions under ruthenium catalysis, see ref 31 and reference 9 therein.
(48) A reaction with diyne **1a** and the catalyst (without alkene) was followed by NMR. A carbenic signal at 15.807 could be detected while product **4a** was being formed (see ref 35).

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