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Alkynyl Halides in Ruthenium(II)-Catalyzed [2+2] Cycloadditions of Bicyclic Alkenes

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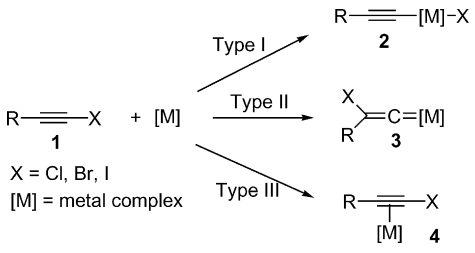
Ru-catalyzed [2+2] cycloadditions between bicyclic alkenes and alkynyl halides were found to occur in moderate to good yields. The presence of the halide moiety greatly enhances the reactivity of the alkyne component in the cycloaddition and can be transformed into a variety of products that are difficult or impossible to obtain by direct cycloaddition.

Introduction

Alkynyl halides are useful building blocks in organic synthesis. Traditionally, alkynyl halides were accessible through the deprotonation of the corresponding terminal alkynes with a strong base, followed by trapping with a halogenating agent.[1] However, several mild and convenient methods have been reported recently and thus have increased the attractiveness of this class of compounds in organic synthesis.[2] The alkynyl halide moiety can be conceived as a dual functionalized molecule in transition-metal-catalyzed reactions (Scheme 1). In the presence of a low-valent transition metal, the metal atom can insert into the carbon–halide bond of the alkynyl halide **1** to form the σ-acetylene–metal complex **2** (Type I). On the other hand, a halovinylidene–metal complex **3** can also be obtained from the alkynyl halide **1** through a 1,2-migration of the halogen (Type II). Finally, the π-system of the acetylene can coordinate to the metal center in an η^2-fashion to form the π-acetylene complex **4** (Type III).



Scheme 1. Potential reactivity pathways of alkynyl halides in transition-metal-catalyzed reactions.

The most extensive studies and applications of alkynyl halides in transition-metal-catalyzed reactions are metal-catalyzed cross-coupling reactions to form carbon–carbon bonds by oxidative insertion of the metal atom into the carbon–halide bond (Type I). Useful building blocks such as enynes,[3] diynes,[4] triynes,[5] and ynamides[6] have been synthesized using this method. The formation of the halovinylidene–metal complex **3** (Type II) is not common, but has been observed when an alkynyl iodide was treated with a tungsten complex, $W(CO)_5(THF)$, to produce an iodovinylidene–tungsten complex which underwent a 6π-electrocyclization.[7] The formation of the π-acetylene complex **4** (Type III) of alkynyl halides are also rare, probably due to the potential problems associated with the oxidative insertion of the metal atom into the carbon–halide bond (Type I). Therefore, very few successful examples of any transition-metal-catalyzed cycloadditions with alkynyl halides, which rely on the formation of the π-acetylene complex **4**, have been reported in the literature (Scheme 2).[8]

We and others have studied various aspects of transition-metal-catalyzed [2+2] cycloadditions between an alkene and an alkyne for the synthesis of cyclobutene rings, including the development of novel catalysts, the study of the intramolecular variant of the reaction, and the investigation on the chemo- and regioselectivity of unsymmetrical substrates.[9–14] More recently, we have demonstrated the first examples of asymmetric induction studies in ruthenium-catalyzed [2+2] cycloadditions between symmetrical bicyclic alkenes and alkynes bearing a chiral auxiliary, and excellent levels of asymmetric induction (up to 98.8% *ee*, after re-

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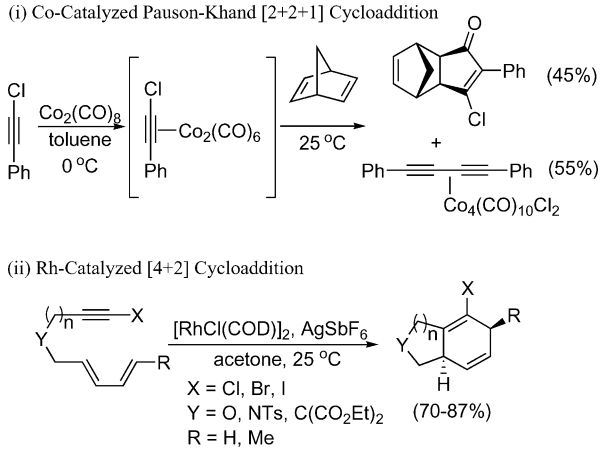
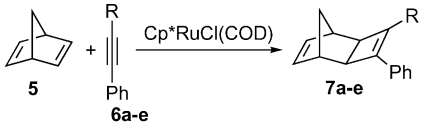


Scheme 2. Transition-metal-catalyzed cycloaddition reactions of alkynyl halides.

moval of the recoverable chiral auxiliary) in the cycloadditions were achieved.[14e] Generally, excellent yields are obtained in the Ru-catalyzed [2+2] cycloadditions between bicyclic alkenes and electron-deficient alkynes (Table 1). However, limitations in the type of suitable alkynes are inevitable, and low yields were obtained when non-electron-deficient or bulky alkynes were used (Table 1). This property of ruthenium-catalyzed [2+2] cycloadditions has, to certain extent, limited the possible cycloadducts affordable through this methodology.

Table 1. Ruthenium-catalyzed [2+2] cycloaddition between norbornadiene and alkynes bearing different functional groups.



5 6a-e 7a-e

Entry	Alkyne	R	Temperature [°C]	Time [h]	Yield [%][a]
1	**6a**	COOEt	60	48	90[b]
2	**6b**	Me	95	90	22[b]
3	**6c**	$SiMe_3$	95	90	0[b]
4	**6d**	Ph	100	120	23[c]
5	**6e**	H	80	16	44[c,d]

[a] Yield of isolated cycloadducts **7**. [b] See ref.[14l] [c] See ref.[9c] [d] Homotrimerization of the terminal alkyne **6e** was also observed, see ref.[9c]

Alkynyl halides are an interesting class of alkynes to explore, because their electron-withdrawing ability could potentially enhance the rate of the [2+2] cycloaddition reaction. The halide moiety could also be used for further functionalization, thereby providing a complementary method for the preparation of those cycloadducts that are difficult or impossible to obtain by direct cycloaddition. In this paper, we have extended our previous preliminary results[8b] and report a full account of the ruthenium-catalyzed [2+2] cycloadditions of bicyclic alkenes with alkynyl halides. This investigation is important, because it provides valuable information on the compatibility and reactivity of alkynyl halides in ruthenium-catalyzed [2+2] cycloadditions, and also provides a method to obtain cycloadducts that are impossible to obtain by direct cycloaddition.

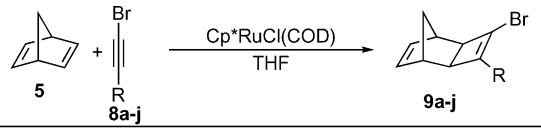
Results and Discussion

Ruthenium-Catalyzed [2+2] Cycloadditions of Norbornadiene (5) with Alkynyl Halides

An initial investigation into various alkynyl bromides was first undertaken to determine the scope of their utility (Table 2). The alkynyl bromides were easily prepared in high yields through the treatment of their corresponding terminal alkynes with *N*-bromosuccinimide (NBS) in the presence of a catalytic amount of silver nitrate.[15] In the presence of 5 mol-% of the catalyst, Cp*RuCl(COD) (Cp* = 1,2,3,4,5-pentamethylcyclopentadienyl, COD = cyclooctadiene), [2+2] cycloadditions between the alkynyl bromide **8a** (R = Ph) and norbornadiene (**5**) occurred smoothly at both 25 and 60 °C to provide the corresponding *exo* cycloadduct **9a** in 78 and 82% yield (Table 2, Entries 1 and 2), respectively, as the only stereoisomer.[16] As the electron-donating capacity of the substituent increased, longer reaction times (R = *p*-Me-C_6H_4, Table 2, Entry 4) and higher temperatures (R = *p*-MeO-C_6H_4, Table 2, Entry 3) were required. It was also observed that steric hindrance associated with the alkyne affected the rate of reaction (compare **8c** vs. **8d** and **8e** vs. **8f**). It should be noted that less reactive alkynes did not allow a full recovery of the net molar balance (i.e. the combined yields of the cycloadduct and the recovered starting material did not add up to 100%). Alkynyl bromides are not very stable under the reaction conditions and subsequently, when the reaction takes place over a long reaction time at higher temperatures, decomposition occurs prior to completion of the cycloadddition reaction. Control experiments showed that, thermal decomposition of the alkynyl bromides was observed upon heating in THF; and no decomposition was detected when the cycloadducts was subjected to the same conditions.

The effect of the halogen group on the cycloaddition reaction was also studied (Table 3).[17] Two series of substrates were investigated (R = Ph and CO_2Et). In the ester series (Table 3, Entries 1–3), the cycloadditions of all the alkynyl chloride, bromide and iodide occurred smoothly even at 25 °C in 1–2 h to give the corresponding cycloadducts in good yields. For the phenyl series, although longer reaction times are required (ca. 48 h) both the cycloadditions of alkynyl chloride and bromide occurred smoothly at 25 and 60 °C to provide the corresponding cycloadducts in good yields (Table 3, Entries 4–7). An uncharacteristic difference in reactivity was observed for 1-iodo-2-phenylethyne (**10d**) (Table 3, Entries 8 and 9). Other than the formation of the usual [2+2] cycloadduct **11d**, a new addition product (**12a**), was also obtained in 26% yield. The structure and stereochemistry of this byproduct **12a** was determined by using mass spectrometry and ^1H, ^{13}C (JMOD), COSY, HSQC

Table 2. Ruthenium-catalyzed [2+2] cycloaddition between norbornadiene and alkynyl bromides.



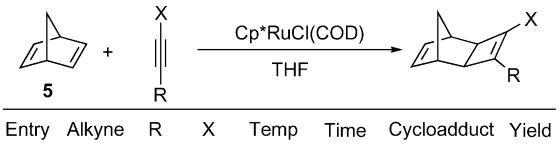
Entry	Alkyne	R	Temperature [°C]	Time [h]	Cycloadduct	Yield [%][a]
1	**8a**	Ph	60	41	**9a**	82
2			25	44		78
3	**8b**	*p*-MeO-C_6H_4	65	72	**9b**	63 (17)
4	**8c**	*p*-Me-C_6H_4	25	72	**9c**	75
5	**8d**	*o*-Me-C_6H_4	65	72	**9d**	20 (16)
6			25	72		28 (38)
7	**8e**	*o*-CF_3-C_6H_4	65	72	**9e**	42
8			40	168		21 (24)
9			25	72		8 (64)
10	**8f**	*m*-F-C_6H_4	65	72	**9f**	75
11			25	72		40 (10)
12	**8g**	*n*Bu	60	72	**9g**	38
13			25	168		32
14	**8h**	CH_2CH_2OTBS	65	69	**9h**	72
15			25	96		52 (15)
16	**8i**	CO_2Et	25	1	**9i**	85
17	**8j**	SO_2Tol	65	65	**9j**	48

[a] Yield of isolated cycloadducts **9**; yield of recovered alkyne in parentheses.

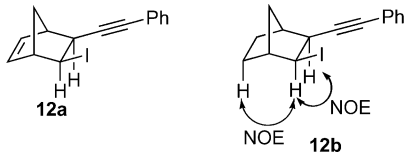
and GOESY NMR experiments.[18–20] The *exo* stereochemistry of both groups was established by GOESY NMR experiments of product **12b**, which was obtained by hydrogenation of **12a**. We believe that the presence of this product can be explained by a combination of two factors. Because the iodide is less electronegative than the bromide and chloride, and the rate of the reaction is increased by utilizing strong electron-withdrawing groups, the cycloaddition occurs at a much slower rate. In addition, because the C–I bond is weaker than both the C–Br and C–Cl bonds, it is easier for the ruthenium atom to oxidatively insert into the C–I bond. To the best of our knowledge, this is the first example of a ruthenium-catalyzed haloalkynylation of alkynyl halide across a double bond.

To estimate the reactivity of alkynyl halides in the ruthenium-catalyzed [2+2] cycloadditions, the relative rate of the ruthenium-catalyzed [2+2] cycloadditions of several alkynes with norbornadiene was measured by competition experiments between the alkyne **6a** (R = Ph, X = COOEt) and other alkynes (Table 4). A typical competition experiment employed 4 equiv. of equimolar amounts of alkyne **6a** (a stock solution of known concentration was prepared for **6a**) and the alkyne **10c** (R = Ph, X = Cl) with 1 equiv. of norbornadiene (**5**) in the presence of 5 mol-% of Cp*RuCl(COD) in THF (large excesses of the alkynes were used in order to approach pseudo-first-order conditions).[21] The reactivity of each alkyne was assessed by evaluation of the product ratio by capillary gas chromatography. The results of these reactivity studies are shown in Table 4. Alkyne **6a** is one of the most reactive alkynes studied so far in ruthenium-catalyzed [2+2] cycloadditions, and it reacts ca. 100 times faster than unactivated alkynes such as **6b** (R = Ph, X = Me). When comparing the reactivity of alkynyl halides **8a** (X = Br) and **10c** (X = Cl) with the alkyne **6a** (X = CO_2Et), cycloadditions with these alkynyl halides appeared to occur even faster than with alkyne **6a**. In fact, the rate of the cycloaddition of **8a** and **10c** with norbornadiene (**5**) were two and nine times faster, respectively, than that of **6a**.

Table 3. Ruthenium-catalyzed [2+2] cycloaddition between norbornadiene and different alkynyl halides.

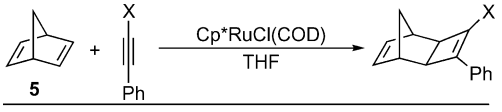


Entry	Alkyne	R	X	Temp [°C]	Time [h]	Cycloadduct	Yield [%][a]
1	**10a**	CO_2Et	Cl	25	1	**11a**	74
2	**8i**		Br	25	1	**9i**	85
3	**10b**		I	25	2	**11b**	89
4	**10c**	Ph	Cl	60	48	**11c**	82
5				25	49		80
6	**8a**		Br	60	48	**9a**	82
7				25	49		78
8	**10d**		I	65	43	**11d**	41[b]
9				25	168		30 (30)[b]



[a] Yield of isolated cycloadducts; yield of recovered alkyne in parerntheses. [b] Side product **12a** was also obtained in 26%.

Table 4. Relative rate of cycloaddition.



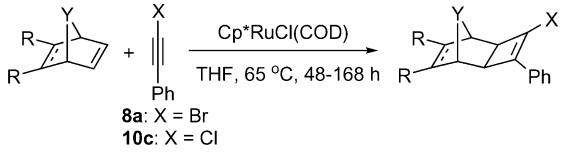
Entry	Alkyne	X	Cycloadduct	Relative rate[a]
1	**6b**	Me	**7b**	0.01
2	**6a**	CO_2Et	**7a**	1
3	**8a**	Br	**9a**	2
4	**10c**	Cl	**11c**	9

[a] Measured from competition experiments, see text; the number indicated is the average number from 3–5 runs.

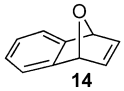
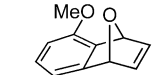
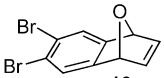
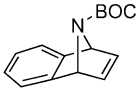
Ruthenium-Catalyzed [2+2] Cycloadditions of Other Symmetrical Bicyclic Alkenes with Alkynyl Halides

The scope of the Ru-catalyzed [2+2] cycloadditions of alkynyl halides with different bicyclic alkenes was also investigated (Table 5).[22] In general, moderate to good yields were obtained in the Ru-catalyzed [2+2] cycloadditions between various bicyclic alkenes (**5**, **13**–**17**) with the alkynyl chloride **10c** and the alkynyl bromide **8a**. The cycloadditions of both the alkynyl chloride **10c** and the alkynyl bromide **8a** with norbornadiene (**5**) gave much higher yields than those with norbornene (**13**) (compare Entries 1 and 2 with Entries 3 and 4). This may be due to the fact that norbornene is less reactive than norbornadiene in Ru-catalyzed [2+2] cycloadditions,[14o] and much longer reaction time was needed for norbornene than for norbornadiene (140 h for the cycloadditions with norbornene and only 48 h for norbornadiene), and thus the thermally unstable alkynyl halides could decompose due to the longer reaction time. Good yield was obtained in the Ru-catalyzed [2+2] cycloadditions between the oxabenzonorbornadiene **14** and the alkynyl chloride **10c** (87%, Entry 5). However, the addition of an electron-donating group (OMe, Entry 7, oxabenzonorbornadiene **15**, 55%) or an electron-withdrawing group (Br, Entry 9, oxabenzonorbornadiene **16**, 41%) on the benzo group of the oxabenzonorbornadiene lead to a significant decrease in the yields. Interestingly, this trend was not observed for different oxabenzonorbornadienes **14**–**16** when the alkynyl bromide **8a** was used as the alkyne partner. In fact, identical yields were observed when the alkynyl bromide **8a** was used in the Ru-catalyzed [2+2] cycloadditions between the oxabenzonorbornadienes **14**–**16** (Entries 6, 8 and 10). The azabenzonorbornadiene **17** also provided good yields of the [2+2] cycloadducts with the alkynyl chloride **10c** and the alkynyl bromide **8a** (Entries 11 and 12). It is worth to mention that due to the two orientations of the BOC group on the nitrogen atom, both cycloadducts **11m** and **11n** were isolated as a mixture of two conformers (one with the BOC group pointing towards the cyclobutene ring, another with the BOC group pointing towards the benzene ring).

Table 5. Ruthenium-catalyzed [2+2] cycloaddition between different bicyclic alkenes and alkynyl halides **8a** and **10c**.



8a: X = Br
10c: X = Cl

Entry	Bicyclic Alkene	Alkyne	X	Cycloadduct	Yield [%][a]
1	 **5**	**10c**	Cl	**11c**	82
2		**8a**	Br	**9a**	82
3	 **13**	**10c**	Cl	**11e**	45
4		**8a**	Br	**11f**	50
5	 **14**	**10c**	Cl	**11g**	87
6		**8a**	Br	**11h**	70
7	 **15**	**10c**	Cl	**11i**	55
8		**8a**	Br	**11j**	70
9	 **16**	**10c**	Cl	**11k**	41
10		**8a**	Br	**11l**	70
11	 **17**	**10c**	Cl	**11m**	88
12		**8a**	Br	**11n**	70

[a] Isolated yield of isolated cycloadducts after column chromatography.

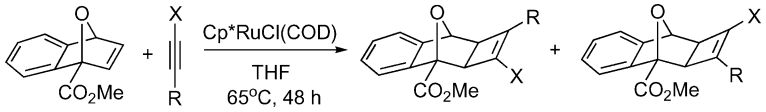
Ruthenium-Catalyzed [2+2] Cycloadditions of Unsymmetrical C1-Substituted Oxabenzonorbornadiene 18 with Alkynyl Halides

Because all the bicyclic alkenes studied above are symmetrical, no regiochemical information in the Ru-catalyzed [2+2] cycloadditions with alkynyl halides can be obtained. To investigate the regiochemical aspects of the Ru-catalyzed [2+2] cycloadditions between unsymmetrical bicyclic alkenes and alkynyl halides, the C1-substituted oxabenzonorbornadiene **18** was prepared.[14m] The Ru-catalyzed [2+2] cycloadditions between the C1-substituted oxabenzonorbornadiene **18** with several alkynyl halides are shown in Table 6.

Several trends can be seen from examining the results of the cycloadditions. The alkynyl halides bearing an unsaturated electron-withdrawing group, such as an ester (CO_2Et, Entries 4–6) and a sulfone (SO_2Tol, Entry 7), show much higher regioselectivity than the alkynyl halides bearing an aromatic ring (Ph, Entries 1–3). The alkynes bearing an ester or a sulfone substituent have ratios of regioisomers ranging from 10:1 to >99:1, whereas those with a Ph group have ratios <2:1. In all cases, the major regioisomer was **19** where the R substituent of the alkyne is placed farther away from the C1 methyl ester. The major regioisomers were determined through 1D GOESY NMR experiments.[20]

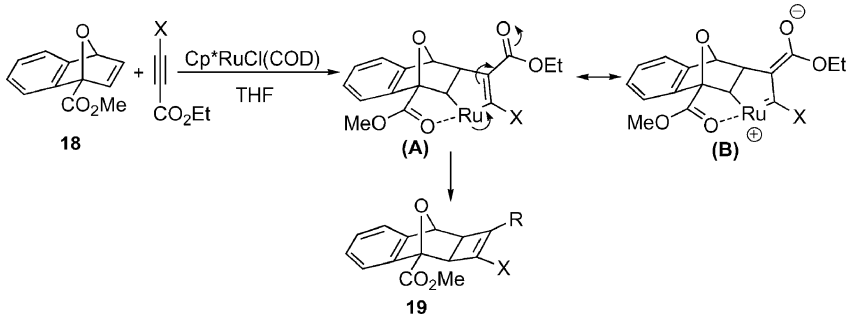
A possible reason for the high regioselectivity with alkynes bearing unsaturated substituents lies in the preferred ruthenapentacycle intermediate (Scheme 3). Oxidative cyclization of the C1-substituted oxabenzonorbornadiene **18** and alkynyl halides bearing an ester group with Cp*RuCl(COD), ruthenapentacycle **A** is most likely formed preferentially due to the ability of the C1 carbonyl functionality of **18** to donate electron density to the ruthenium

Table 6. Ruthenium-catalyzed [2+2] cycloaddition between C1-substituted oxabenzonorbornadiene **18** with alkynyl halides.



Entry	Alkyne	R	X		Regioselectivity[a] 19 : 20	Yield [%][b,c]
1	**10c**	Ph	Cl	**(19a : 20a)**	1.2 : 1	31
2	**8a**		Br	**(19b : 20b)**	1.7 : 1	39
3	**10d**		I	**(19c : 20c)**	1.4: 1	41
4	**10a**	CO_2Et	Cl	**(19d : 20d)**	61 : 1	44
5	**8i**		Br	**(19e : 20e)**	18 : 1	42
6	**10b**		I	**(19f : 20f)**	10 : 1	60
7	**8j**	SO_2Tol	Br	**(19g : 20g)**	>99 : 1[d]	21

[a] The ratio of regioisomers was determined by GC or 400 MHz ^{1}H NMR spectroscopy; the regiochemistry of the cycloadducts were determined by ^{1}D GOESY NMR experiments, see text. [b] Yield of isolated cycloadducts. [c] Other side products formed from the isomerization of oxanorbornadiene **18** and cyclotrimerization of the alkynyl halides were also observed, see text. [d] No minor regioisomer can be detected by 400 MHz ^{1}H NMR spectroscopy.



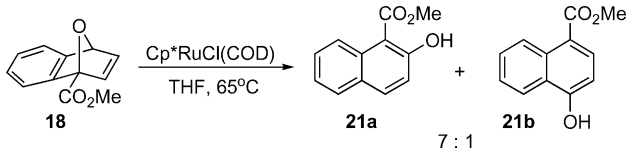
Scheme 3. Possible explanation of regioselectivity.

metal center. The alkyne is preferentially oriented with the ester functionality further from the metal atom, as it can then participate in resonance, forming **B**, to delocalize the electron density and therefore stabilize the intermediate ruthenapentacycle. Reductive elimination of **A** leads to the major regioisomer **19**.

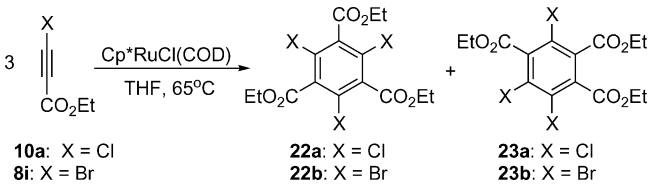
Another trend in the regioselectivity can be observed when comparing the reactions with alkynes bearing the ethyl ester moiety (Entries 4–6). As the halide moves down the periodic table (Cl to Br to I), the regioselectivity decreases, with the alkynyl chloride **10a** giving the best ratio of the series at 61:1; however, the regioselectivity was still good in all cases. A possible explanation of this trend revolves around the size of the halide; as the halide atom becomes larger moving from chloride to iodide, sterics may begin to play a larger role, resulting in more of cycloadduct **20** being produced with the halide atom further away from the C1 methyl ester of **18**.

The yields that were obtained in the cycloaddition reactions with the oxabenzonorbornadiene **18** were all fairly low, with the highest yield at 60% for the alkyne **10b** (Entry 6). Apart from the decomposition of alkynyl halides at higher reaction temperature, two other factors contributing to the low yields of the cycloadditions: isomerization of the C1-substituted oxabenzonorbornadiene **18** to the corresponding naphthols **21** (Scheme 4) and the cyclotrimerization of alkynyl halides to the corresponding benzene derivatives **22** and **23** (Scheme 5). In the majority of the reactions carried out, both the alkyne and the alkene components were involved in the formation of side products. In every reaction at elevated temperatures, the oxabenzonorbornadiene **18** isomerized to the corresponding naphthols **21** (Scheme 4). Methyl 2-hydroxy-1-naphthoate (**21a**) was determined to be the major isomer through comparison with literature NMR spectra as well as by the characteristic sharp singlet ^{1}H NMR signal found at δ = 11.98 ppm, corresponding to an intramolecular hydrogen-bonded aryl hydroxy proton. The naphthol **21a** was found to be obtained in a 7:1 ratio with methyl 4-hydroxy-1-naphthoate (**21b**). Although this isomerization was seen in every reaction above room temperature, the alkene component was used in excess, and the amount of isomerization observed may not

have affected the yield substantially. This isomerization was not observed when the reaction was run at room temperature.



Scheme 4. Isomerization of oxabenzonorbornadiene **18**.

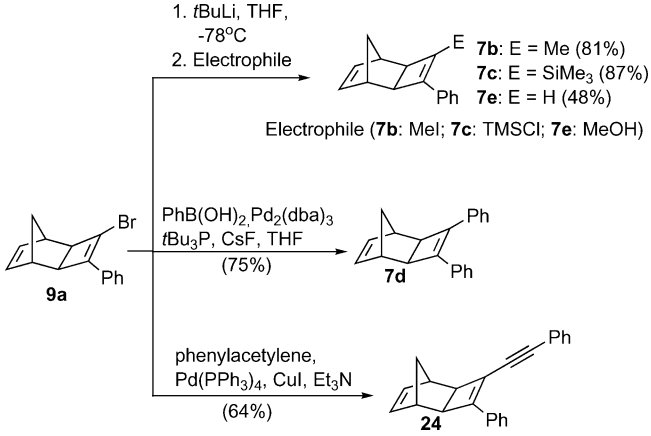


Scheme 5. Cyclotrimerization of alkynyl halides **10a** and **8i**.

The side products formed from the alkyne component could be a much larger contributor to the diminished yields of the reaction. Side products involving just the alkynyl halide proved to be problematic in the cycloadditions with alkynes bearing the ester moiety (Entries 4–6). Both the alkynyl chloride **10a** and the bromide **8i** produced a substantial amount of the trimerized alkyne benzene products **22** and **23** in almost a 1:1 ratio (Scheme 5). During the Ru-catalyzed [2+2] cycloaddition of the oxabenzonorbornadiene **18** with the alkynyl halides **10a** and **8i** (Table 6, Entries 4 and 5), the trimerized side products **22** and **23** were obtained in almost a 1:1 ratio with the corresponding cycloadducts. For the alkynyl chloride **10a**, apart from obtaining 44% of the [2+2] cycloadducts **19d** and **20d**, the benzenes **22a** and **23a** were also obtained in a 38% yield (**22a**/**23a** ≈ 1:1), based on starting alkyne. For the alkynyl bromide **8i**, apart from obtaining 42% of the [2+2] cycloadducts **19e** and **20e**, the benzenes **22b** and **23b** were also obtained in a 44% yield (**22b**/**23b** ≈ 1:1). To ensure these trimerized products were a result of the alkynes interacting with the catalyst alone, control reactions were carried out without the presence of the oxabenzonorbornadiene **18**. It was found that the alkynes were converted into the trimerized benzene products with almost quantitative yields. Through various experiments, it was also found that the alkynyl chloride **10a** is more prone to the trimerization. When the cycloaddition between the oxabenzonorbornadiene **18** and the alkynyl chloride **10a** was attempted at room temperature, only the trimerized benzene products were obtained, and no improvement in the cycloadduct yield was observed. However, when the cycloaddition between oxabenzonorbornadiene **18** and the alkynyl bromide **8i** was carried out at room temperature, no trimerized benzenes **22b**/**23b** were observed, and the yield of the cycloadducts **19e** and **20e** improved to 57%. As well, it was also found in the control experiments that the alkynyl chloride requires less time to convert completely to the benzenes when compared to the alkynyl bromide. The alkynyl iodide **10b** was not found to undergo the trimerization. This could be attributed to the lower electronegativity of the iodide as well as steric interactions due to its size. The lack of trimerization is reflected in the large improvement in the yield obtained for the cycloaddition when compared to the chloride and bromide analogs (compare Entry 6 with Entries 4 and 5 in Table 6).

Synthetic Applications of Halogenated [2+2] Cycloadducts

In order to illustrate the synthetic usefulness of the resulting halogenated cycloadducts, the cycloadduct **9a** was treated under a variety of reaction conditions to achieve further functionalization. As shown in Scheme 6, lithium/halide exchange followed by trapping with various electrophiles led to the products **7b**,**c**,**e** in moderate to good yields. Suzuki coupling between **9a** and phenylboronic acid provided **7d** in 75%, and Sonogashira coupling between **9a** and phenylacetylene gave **24** in 64%. As previously shown in Table 1, these products are difficult or impossible to obtain by direct cycloaddition.



Scheme 6. Functionalization of cycloadduct **9a**.

Conclusions

We have demonstrated the first examples of Ru-catalyzed [2+2] cycloadditions between alkynyl halides and bicyclic alkenes (yields up to 89%). The presence of the halide moiety is compatible in the ruthenium-catalyzed [2+2] cycloadditions and greatly enhances the reactivity of the alkyne component in the cycloaddition. The halide moiety could also be used for further functionalization, thereby providing a complementary method for the preparation of those cycloadducts that are difficult or impossible to obtain by direct cycloaddition. We have investigated the regiochemical aspects of the Ru-catalyzed [2+2] cycloadditions between the unsymmetrical C1-substituted oxabenzonorbornadiene **18** and several alkynyl halides. A high level of regioselectivities was observed with alkynyl halides bearing an unsaturated electron-withdrawing group such as an ester or a sulfone. During this study, we have also discovered a novel

haloalkynylation reaction between 1-iodo-2-phenylethyne and norbornadiene catalyzed by the catalyst Cp*RuCl(COD). Further investigation of the origin, reactivity and application of this novel type of ruthenium-catalyzed haloalkynylation is ongoing in our laboratory.

Experimental Section

General: All reactions were carried out under dry nitrogen at ambient temperature unless otherwise stated. Standard column chromatography was performed on 230–400 mesh silica gel (obtained from Silicycle) by using flash column chromatography techniques.[23] Analytical thin-layer chromatography (TLC) was performed on Merck precoated silica gel 60 F_{254} plates. All glassware was flame-dried under dry nitrogen or oven-dried overnight. Infrared spectra were taken with a Bomem MB-100 or Nicolet FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded with Bruker Avance 300, 400 or 600 spectrometers. Chemical shifts for ^{1}H NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent resonance as the internal standard (chloroform: δ = 7.26 ppm). Chemical shifts for ^{13}C NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent as the internal standard (deuteriochloroform: δ = 77.0 ppm). High-resolution mass spectra were recorded by McMaster Regional Centre for Mass Spectrometry at McMaster University, Hamilton, Ontario. Elemental analyses were performed by Canadian Microanalytical Service Ltd., British Columbia or by Quantitative Technologies Inc., New Jersey. Unless stated otherwise, commercial reagents were used without purification. Solvents were purified by distillation under dry nitrogen from potassium/benzophenone (THF) and from 4 Å molecular sieves (Et_3N). Norbornadiene (**5**) and norbornene (**13**) were purchased from Aldrich. The alkynyl halides **8a**–**c**,[2d,15] **8e**,[15,24] **8g**,[15,25] **8i**,[15,26] **8j**,[15,27] **10a**,[17b] **10b**,[15,28] **10c**,[29] **10d**,[15,30] the bicyclic alkenes **14**–**18**,[31,32] and [Cp*RuCl(COD)][33] were prepared according to literature procedures.

Synthesis of Alkynyl Bromides

General Procedure (A) for the Synthesis of the Alkynyl Bromides: *N*-Bromosuccinimide (NBS, 1.2 equiv.) and silver nitrate (0.13 equiv.) were added to a solution of a terminal alkyne (1 equiv.) in acetone (10 mL). The reaction mixture was stirred at 25 °C for 15 min to 2 h. Upon completion, the reaction mixture was poured into an ice/water bath, and the resulting aqueous solution was extracted three times with diethyl ether. The organic phases were combined, washed with brine, dried with $MgSO_4$, filtered, and concentrated by rotary evaporation. The crude product was purified by column chromatography (hexanes or ethyl acetate/hexanes mixture) to provide the alkynyl halides.

1-Bromo-2-(2-methylphenyl)ethyne (8d): According to the above procedure (A) with 1-ethynyltoluene (0.5 mL, 3.969 mmol), NBS (861.5 mg, 4.788 mmol), and $AgNO_3$ (69.1 mg, 0.407 mmol) in acetone (10 mL), the reaction mixture was stirred at 25 °C for 1 h. The crude product was purified by column chromatography (EtOAc/hexanes, 1:99) to provide **8d** (645.1 mg, 3.307 mmol, 83%) as a yellow oil. R_f = 0.46 (hexanes). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.42 (d, 1 H, J = 7.9 Hz), 7.20 (m, 2 H), 7.13 (t, 1 H, J = 7.2 Hz), 2.44 (s, 3 H). ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 140.9, 132.4, 129.4, 128.6, 125.5, 122.5, 79.1, 52.8, 20.6 ppm. This is a known compound and the spectroscopic data are identical to those reported in the literature.[34]

1-Bromo-2-(3-fluorophenyl)ethyne (8f): According to the above general procedure (A) with 1-ethynyl-3-fluorobenzene (0.5 mL, 4.324 mmol), NBS (935.2 mg, 5.197 mmol), and $AgNO_3$ (98.1 mg, 0.578 mmol) in acetone (10 mL), the reaction mixture was stirred at 25 °C for 2 h. The crude product was purified by column chromatography (hexanes) to provide **8f** (724.4 mg, 3.640 mmol, 84%) as a yellow oil. R_f = 0.66 (hexanes). IR (neat, NaCl): $\tilde{\nu}$ = 3073 (w), 2228 (w), 2196 (m), 1783 (w), 1620 (w), 1608 (s), 1582 (s), 1485 (s), 1435 (s), 1271 (s), 1144 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.14 (m, 4 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 162.2 (d, J = 247.0 Hz), 129.9 (d, J = 8.6 Hz), 127.9, 124.2 (d, J = 9.6 Hz), 118.8 (d, J = 23.0 Hz), 116.1 (d, J = 21.2 Hz), 78.9, 51.2 ppm. HRMS: calcd. for C_8H_4FBr 197.9480, found 197.9492.

1-Bromo-4-(*tert*-butyldimethylsilyloxy)butyne (8h): According to the above general procedure (A) with 4-(*tert*-butyldimethylsilyloxy)-butyne (401.3 mg, 2.177 mmol), NBS (439.1 mg, 2.440 mmol), and $AgNO_3$ (61.0 mg, 0.310 mmol) in acetone (10 mL), the reaction mixture was stirred at 25 °C for 15 min. The crude product was purified by column chromatography (EtOAc/hexanes, 1:19) to provide **8h** (433.5 mg, 1.647 mmol, 76%) as a colorless oil. R_f = 0.60 (EtOAc/hexanes, 1:19). IR (neat): $\tilde{\nu}$ = 2956 cm^{-1}. (s), 2930 (s), 2883 (s), 2858 (s), 2739 (w), 2711 (w), 1254 (m), 1112 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.73 (t, J = 7.0 Hz, 2 H), 2.41 (t, J = 7.0 Hz, 2 H), 0.90 (s, 9 H), 0.06 (s, 6 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 77.5, 61.5, 39.0, 25.8, 24.0, 18.3, –5.3 ppm. HRMS: calcd. for $C_{10}H_{19}BrOSi$ 262.0389, found 262.0395.

Ruthenium-Catalyzed [2+2] Cycloadditions

General Procedure (B) for the Ru-Catalyzed [2+2] Cycloaddition Between Norbornadiene and Alkynyl Halides: A mixture of norbornadiene (**5**, 3–5 equiv.), alkynyl halide (1 equiv.) and THF in an oven-dried vial was added by a cannula to an oven-dried screw-cap vial containing Cp*RuCl(COD) (weighed out from a dry box, 5–10 mol-%) under nitrogen. The reaction mixture was stirred in the dark at 25–65 °C for 1–168 h. The crude product was purified by column chromatography to give the cycloadduct.

Cycloadduct 9a (Table 2, Entry 1): According to the above general procedure (B) with norbornadiene (**5**, 93.2 mg, 1.01 mmol), alkynyl bromide **8a** (37.2 mg, 0.206 mmol), THF (0.30 mL), and Cp*RuCl(COD) (3.6 mg, 0.009 mmol). The reaction mixture was stirred in the dark at 60 °C for 48 h. The crude product was purified by column chromatography (hexanes) to give the cycloadduct **9a** (46.2 mg, 0.169 mmol, 82%) as a pale yellow oil. R_f = 0.57 (hexanes). GC (HP-1 column): retention time = 13.453 min. IR (neat): $\tilde{\nu}$ = 3060 (s), 2971 (s), 2949 (s), 2875 (w), 1947 (w), 1877 (w), 1801 (w), 1748 (w), 1629 (m), 1598 (w), 1489 (s), 1447 (s), 1320 (s), 1253 (s), 1291 (s), 1253 (s), 1220 (m), 1190 (s), 1117 (w), 1083 (w), 1025 (w), 996 (w), 931 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.72 (dm, J = 7.3 Hz, 2 H), 7.40 (t, J = 7.3 Hz, 2 H), 7.33 (dm, J = 7.3 Hz, 1 H), 6.23 (m_{ABX}, 2 H), 2.88 (d, J = 3.6 Hz, 1 H), 2.77 (m, 1 H), 2.76 (s, 1 H), 2.66 (br. s, 1 H), 1.47 (q_{AB}, ^2J = 9.4 Hz, 2 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 145.6, 136.5, 135.9, 132.1, 128.42, 128.38, 125.6, 114.4, 52.2, 46.4, 40.2, 39.4, 38.4 ppm. HRMS: calcd. for $C_{15}H_{13}Br$ 272.0201, found 272.0180.

Cycloadduct 9b (Table 2, Entry 3): According to the above general procedure (B) with norbornadiene (**5**, 150 μL, 1.39 mmol), alkynyl bromide **8b** (34.6 mg, 0.163 mmol), THF (0.30 mL), and Cp*RuCl(COD) (5.1 mg, 0.013 mmol). The reaction mixture was stirred in the dark at 65 °C for 72 h. The crude product was purified by column chromatography (EtOAc/hexanes, 1:99) to give the cycloadduct **9b** (31.2 mg, 0.103 mmol, 63%) as a white solid. M.p. 37–38 °C. R_f = 0.41 (EtOAc/hexanes, 1:19). IR (neat, NaCl): $\tilde{\nu}$ =

3127 (w), 3059 (m), 3034 (w), 2970 (s), 2949 (s), 2874 (w), 2836 (m), 2049 (w), 1887 (w), 1632 (m), 1603 (s), 1505 (s), 1461 (m), 1320 (s), 1301 (s), 1257 (s), 1174 (s), 931 (s), 832 (s), 710 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.65 (m, 2 H), 6.92 (m, 2 H), 6.21 (m, 2 H), 3.83 (s, 3 H), 2.83 (d, J = 3.7 Hz, 1 H), 2.73 (d, J = 3.7 Hz, 1 H), 2.72 (br. s, 1 H), 2.63 (br. s, 1 H), 1.47 (d, J = 9.3 Hz, 1 H), 1.42 (d, J = 9.3 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 159.6, 145.0, 136.3, 135.9, 127.1, 125.1, 113.8, 111.5, 55.3, 52.0, 46.2, 40.2, 39.3, 38.5 ppm. HRMS: calcd. for $C_{16}H_{15}OBr$ 302.0306, found 302.0318.

Cycloadduct 9c (Table 2, Entry 4): According to the above general procedure (B) with norbornadiene (**5**, 50 μL, 0.463 mmol), alkynyl bromide **8c** (30.0 mg, 0.153 mmol), THF (0.30 mL), and Cp*RuCl(COD) (4.1 mg, 0.011 mmol). The reaction mixture was stirred in the dark at 25 °C for 72 h. The crude product was purified by column chromatography (hexanes) to give the cycloadduct **9c** (32.8 mg, 0.114 mmol, 75%) as a yellow solid. M.p. 30 °C; R_f = 0.56 (hexanes). IR (neat, NaCl): $\tilde{\nu}$ = 3127 (w), 3059 (m), 3025 (m), 2972 (s), 2948 (s), 2875 (m), 1904 (w), 1791 (w), 1630 (m), 1608 (m), 1565 (m), 1506 (s), 1450 (s), 1319 (s), 1291 (s), 1255 (s), 1220 (m), 1191 (s), 931 (s), 819 (s), 707 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.61 (d, J = 8.1 Hz, 2 H), 7.20 (d, J = 7.9 Hz, 2 H), 6.22 (m, 2 H), 2.86 (d, J = 3.7 Hz, 1 H), 2.75 (d, J = 3.5 Hz, 1 H), 2.74 (br. s, 1 H), 2.64 (br. s, 1 H), 2.36 (s, 3 H), 1.47 (d, J = 9.3 Hz, 1 H), 1.42 (d, J = 9.3 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 145.5, 138.4, 136.4, 135.9, 129.4, 129.1, 125.6, 113.1, 52.1, 46.3, 40.2, 39.4, 38.5, 21.5 ppm. HRMS: calcd. for $C_{16}H_{15}Br$ 286.0357, found 286.0365.

Cycloadduct 9d (Table 2, Entry 6): According to the above general procedure (B) with norbornadiene (**5**, 50 μL, 0.463 mmol), alkynyl bromide **8d** (34.1 mg, 0.175 mmol), THF (0.30 mL), and Cp*RuCl(COD) (3.4 mg, 0.009 mmol). The reaction mixture was stirred in the dark at 25 °C for 72 h. The crude product was purified by column chromatography (hexanes) to give the cycloadduct **9d** (14.0 mg, 0.0487 mmol, 28%) as a yellow oil. R_f = 0.32 (hexanes). IR (neat, NaCl): $\tilde{\nu}$ = 3127 (w), 3060 (m), 3017 (m), 2971 (s), 2951 (s), 2875 (m), 1915 (w), 1622 (w), 1600 (w), 1564 (w), 1485 (s), 1449 (s), 1319 (s), 1293 (s), 1247 (s), 1221 (s), 1193 (s), 927 (s), 886 (s), 803 (m), 760 (s), 722 (s), 711 (s), 695 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.64 (m, 1 H), 7.21 (m, 3 H), 6.22 (m, 2 H), 3.01 (d, J = 3.6 Hz, 1 H), 2.75 (d, J = 3.3 Hz, 1 H), 2.68 (br. s, 1 H), 2.60 (br. s, 1 H), 2.45 (s, 3 H), 1.58 (d, J = 9.3 Hz, 1 H), 1.44 (d, J = 9.3 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 147.6, 136.5, 136.1, 136.0, 131.8, 130.8, 128.2, 127.8, 125.6, 116.5, 52.4, 50.0, 40.1, 39.5, 39.2, 21.1 ppm. HRMS: calcd. for $C_{16}H_{15}Br$ 286.0357, found 286.0352.

Cycloadduct 9e (Table 2, Entry 7): According to the above general procedure (B) with norbornadiene (**5**, 39 μL, 0.362 mmol), alkynyl bromide **8e** (33.8 mg, 0.136 mmol), THF (0.30 mL), and Cp*RuCl(COD) (4.1 mg, 0.011 mmol). The reaction mixture was stirred in the dark at 65 °C for 72 h. The crude product was purified by column chromatography (hexanes) to give the cycloadduct **9e** (19.4 mg, 0.0569 mmol, 42%) as a colorless oil. R_f = 0.48 (hexanes). IR (neat, NaCl): $\tilde{\nu}$ = 3129 (w), 3063 (m), 2976 (s), 2877 (m), 1941 (w), 1831 (w), 1604 (m), 1573 (w), 1485 (m), 1452 (m), 1317 (s), 1242 (m), 1172 (s), 1130 (s), 1039 (s), 933 (s), 762 (s), 698 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.80 (d, J = 7.7 Hz, 1 H), 7.70 (d, J = 7.9 Hz, 1 H), 7.56 (t, J = 7.6 Hz, 1 H), 7.43 (t, J = 7.7 Hz, 1 H), 6.21 (m, 2 H), 3.12 (br. s, 1 H), 2.77 (d, J = 3.4 Hz, 1 H), 2.69 (s, 1 H), 2.53 (s, 1 H), 1.50 (d, J = 9.4 Hz, 1 H), 1.45 (d, J = 9.4 Hz, 1 H) ppm. ^{13}C NMR (^{13}C, $CDCl_3$, 100 MHz): δ = 145.6, 136.9, 135.9, 131.6, 131.2, 130.2, 128.0, 127.1 (q, J = 30.7 Hz), 126.2 (q, J = 5.8 Hz), 123.9 (q, J = 273.3 Hz), 119.7, 52.1, 50.2 (q, J = 3.6 Hz), 40.2, 39.2, 39.0 ppm. HRMS: calcd. for $C_{16}H_{12}F_3Br$ 340.0074, found 340.0070.

Cycloadduct 9f (Table 2, Entry 10): According to the above general procedure (B) with norbornadiene (**5**, 270 μL, 2.50 mmol), alkynyl bromide **8f** (61.0 mg, 0.307 mmol), THF (0.30 mL), and Cp*RuCl(COD) (5.7 mg, 0.015 mmol). The reaction mixture was stirred in the dark at 65 °C for 72 h. The crude product was purified by column chromatography (hexanes) to give the cycloadduct **9f** (66.9 mg, 0.230 mmol, 75%) as a yellow oil. R_f = 0.40 (hexanes). IR (neat, NaCl): $\tilde{\nu}$ = 3128 (w), 3062 (m), 2973 (s), 2950 (s), 2876 (m), 1933 (w), 1856 (w), 1781 (w), 1743 (w), 1608 (s), 1582 (s), 1481 (s), 1444 (s), 1320 (s), 1265 (s), 1203 (s), 1174 (s), 1156 (s), 955 (s), 873 (s), 849 (s), 785 (s), 711 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.37 (m, 3 H), 7.02 (m, 1 H), 6.23 (m, 2 H), 2.86 (d, J = 3.7 Hz, 1 H), 2.77 (d, J = 3.7 Hz, 1 H), 2.75 (br. s, 1 H), 2.66 (br. s, 1 H), 1.45 (s, 2 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 162.8 (d, J = 245.9 Hz), 144.6, 136.4, 135.9, 134.1 (d, J = 7.8 Hz), 130.0 (d, J = 8.3 Hz), 121.3 (d, J = 2.6 Hz), 116.2, 115.2 (d, J = 21.4 Hz), 112.2 (d, J = 22.0 Hz), 52.2, 46.4, 40.1, 39.3, 38.3 ppm. HRMS: calcd. for $C_{15}H_{12}FBr$ 290.0106, found 290.0102.

Cycloadduct 9g (Table 2, Entry 12): According to the above general procedure (B) with norbornadiene (**5**, 60 μL, 0.556 mmol), alkynyl bromide **8g** (30.6 mg, 0.190 mmol), THF (0.30 mL), and Cp*RuCl(COD) (5.6 mg, 0.015 mmol). The reaction mixture was stirred in the dark at 60 °C for 72 h. The crude product was purified by column chromatography (hexanes) to give the cycloadduct **9g** (18.3 mg, 0.072 mmol, 38%) as a yellow oil. R_f = 0.62 (hexanes). IR (neat, NaCl): $\tilde{\nu}$ = 3060 (w), 2958 (s), 2931 (s), 2872 (m), 1652 (w), 1456 (m), 1379 (w), 1293 (w), 1241 (w), 1219 (w), 1192 (w), 1156 (w), 1059 (w), 960 (w), 695 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 6.13 (m, 2 H), 2.58 (m, 1 H), 2.52 (br. s, 1 H), 2.50 (br. s, 1 H), 2.46 (d, J = 3.5 Hz, 1 H), 2.07 (m, 2 H), 1.40 (m, 6 H), 0.92 (t, J = 7.3 Hz, 3 H) ppm. ^{13}C NMR (^{13}C, $CDCl_3$, 100 MHz): δ = 151.1, 136.3, 135.8, 113.9, 52.1, 47.9, 40.0, 38.9, 38.1, 28.7, 27.0, 22.8, 13.8 ppm. HRMS: calcd. for $C_{13}H_{17}Br$ 252.0514, found 252.0520.

Cycloadduct 9h (Table 2, Entry 14): According to the above general procedure (B) with norbornadiene (**5**, 65 μL, 0.60 mmol), alkynyl bromide **8h** (56.8 mg, 0.216 mmol), THF (0.50 mL), and Cp*RuCl(COD) (6.2 mg, 0.016 mmol). The reaction mixture was stirred in the dark at 65 °C for 69 h. The crude product was purified by column chromatography (EtOAc/hexanes, 1:49) to give the cycloadduct **9h** (55.2 mg, 0.155 mmol, 72%) as a colorless oil. R_f = 0.60 (EtOAc/hexanes, 1:19). IR (neat): $\tilde{\nu}$ = 3129 cm^{-1}. (w), 3061 (w), 2954 (s), 2930 (s), 2885 (m), 2857 (s), 1255 (s), 1102 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 6.13 (br. s, 2 H), 3.731 (t, J = 6.7 Hz, 1 H), 3.725 (t, J = 6.8 Hz, 1 H), 2.60 (br. s, 1 H), 2.49–2.52 (m, 3 H), 2.30 (t, J = 6.8 Hz, 2 H), 1.45 (br. d, J = 9.2 Hz, 1 H), 1.38 (br. d, J = 9.2 Hz, 1 H), 0.90 (s, 9 H), 0.06 (s, 6 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 148.5, 136.4, 135.7, 115.7, 60.3, 52.5, 48.4, 40.1, 38.9, 38.0, 31.2, 25.9, 18.2, –5.3 ppm. HRMS: calcd. for $C_{17}H_{27}BrOSi$ 354.1015, found 354.1010.

Cycloadduct 9i (Table 2, Entry 16): According to the above general procedure (B) with norbornadiene (**5**, 47 μL, 0.44 mmol), alkynyl bromide **8i** (26.0 mg, 0.147 mmol), THF (0.30 mL), and Cp*RuCl(COD) (4.4 mg, 0.017 mmol). The reaction mixture was stirred in the dark at 25 °C for 1 h. The crude product was purified by column chromatography (EtOAc/hexanes, 1:19) to give the cycloadduct **9i** (33.6 mg, 0.125 mmol, 85%) as a colorless oil. R_f = 0.38 (EtOAc/hexanes, 1:19). IR (neat): $\tilde{\nu}$ = 3129 (w), 3062 (m), 2979 (s), 2958 (s), 1904 (m), 2882 (m), 1714 (s), 1623 (s), 1454 (m), 1304

(s), 1198 (s), 1133 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 6.21 (dd, J = 5.5, 3.1 Hz, 1 H), 6.16 (dd, J = 5.4, 3.1 Hz, 1 H), 4.23 (q, J = 7.1 Hz, 2 H), 2.74 (m, 2 H), 2.67 (m, 1 H), 2.61 (br. s, 1 H), 1.45 (br. d, J = 9.6 Hz, 1 H), 1.36 (br. d, J = 9.7 Hz, 1 H), 1.32 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 161.2, 139.6, 137.1, 135.3, 133.1, 60.4, 52.7, 46.8, 39.9, 38.8, 37.8, 14.2 ppm. HRMS: calcd. for $C_{12}H_{13}BrO_2$ 268.0099, found 268.0089; $C_{12}H_{13}BrO_2$ (269.14): calcd. C 53.55, H 4.87; found C 53.72; H 4.99.

Cycloadduct 9j (Table 2, Entry 17): According to the above general procedure (B) with norbornadiene (**5**, 60 μL, 0.56 mmol), alkynyl bromide **8j** (46.0 mg, 0.18 mmol), THF (0.30 mL), and Cp*RuCl(COD) (6.4 mg, 0.017 mmol). The reaction mixture was stirred in the dark at 65 °C for 65 h. The crude product was purified by column chromatography (EtOAc/hexanes, 1:19) to give the cycloadduct **9j** (30.3 mg, 0.086 mmol, 48%) as a colorless oil. R_f = 0.52 (EtOAc/hexanes, 1:4). IR (neat): $\tilde{\nu}$ = 3060 (m), 2974 (s), 2956 (s), 2926 (m), 2881 (m), 1580 (s), 1315 (s), 1156 (s)1089 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.86 (d, J = 8.3 Hz, 2 H), 7.36 (d, J = 8.3 Hz, 2 H), 6.13 (m, 2 H), 2.86 (br. d, J = 3.5 Hz, 1 H), 2.67 (br. d, J = 3.5 Hz, 1 H), 2.62 (br. s, 1 H), 2.58 (br. s, 1 H), 2.45 (s, 3 H), 1.36 (dm, J = 9.9 Hz, 1 H), 1.12 (dm, J = 9.9 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 145.4, 145.0, 136.9, 136.4, 135.5, 131.7, 130.0, 128.0, 52.5, 48.9, 39.7, 38.8, 38.7, 21.7 ppm. $C_{16}H_{15}BrO_2S$ (351.26): calcd. C 54.71, H 4.30; found C 54.58, H 4.42.

Cycloadduct 11a (Table 3, Entry 1): According to the above general procedure (B) with norbornadiene (**5**, 60 μL, 0.56 mmol), alkynyl chloride **10a** (21.5 mg, 0.162 mmol), THF (0.30 mL), and Cp*RuCl(COD) (4.3 mg, 0.011 mmol). The reaction mixture was stirred in the dark at 25 °C for 1 h. The crude product was purified by column chromatography (EtOAc/hexanes, 1:19) to give the cycloadduct **11a** (27.1 mg, 0.121 mmol, 74%) as a colorless oil. R_f = 0.38 (EtOAc/hexanes, 1:19). IR (neat): $\tilde{\nu}$ = 3133 (w), 3062 (m), 2979 (s), 2883 (m), 1716 (s), 1455 (s), 1306 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 6.22 (dd, J = 5.5, 3.0 Hz, 1 H), 6.16 (dd, J = 5.5, 3.0 Hz, 1 H), 4.23 (q, J = 7.1 Hz, 2 H), 2.74 (br. s, 1 H), 2.65 (m, 2 H), 2.61 (m, 1 H), 1.46 (br. d, J = 9.6 Hz, 1 H), 1.39 (br. d, J = 9.6 Hz, 1 H), 1.32 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 161.0, 143.5, 137.3, 135.3, 134.8, 60.4, 51.5, 44.1, 39.8, 39.0, 37.6, 14.2 ppm. HRMS: calcd. for $C_{12}H_{13}ClO_2$ 224.0604, found 224.0604.

Cycloadduct 11b (Table 3, Entry 3): According to the above general procedure (B) with norbornadiene (**5**, 35 μL, 0.32 mmol), alkynyl iodide **10b** (24.9 mg, 0.111 mmol), THF (0.30 mL), and Cp*RuCl(COD) (3.2 mg, 0.0084 mmol). The reaction mixture was stirred in the dark at 25 °C for 2 h. The crude product was purified by column chromatography (EtOAc/hexanes, 1:19) to give the cycloadduct **11b** (31.2 mg, 0.0987 mmol, 89%) as a colorless oil. R_f = 0.63 (EtOAc/hexanes, 1:4). IR (neat): $\tilde{\nu}$ = 3124 (w), 3058 (m), 2980 (s), 2910 (m), 2898 (m), 1708 (s), 1606 (s), 1303 (s), 1256 (s), 1132 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 6.20 (dd, J = 5.5, 3.0 Hz, 1 H), 6.17 (dd, J = 5.4, 3.0 Hz, 1 H), 4.23 (q, J = 7.1 Hz, 2 H), 2.89 (br. d, J = 3.5 Hz, 1 H), 2.72 (br. s, 1 H), 2.66 (br. d, J = 3.5 Hz, 1 H), 2.51 (br. s, 1 H), 1.42 (dm, J = 9.6 Hz, 1 H), 1.32 (t, J = 7.1 Hz, 3 H), 1.28 (dm, J = 9.6 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 161.6, 147.6, 136.8, 135.3, 108.8, 60.4, 53.7, 50.1, 40.0, 38.6, 38.1, 14.2 ppm. $C_{12}H_{13}IO_2$ (316.14): calcd. C 45.59, H 4.14; found C 45.68, H 4.01.

Cycloadduct 11c (Table 3, Entry 4): According to the above general procedure (B) with norbornadiene (**5**, 66.0 mg, 0.716 mmol), alkynyl chloride **10c** (29.6 mg, 0.217 mmol), THF (0.35 mL), and Cp*RuCl(COD) (5.4 mg, 0.014 mmol). The reaction mixture was stirred in the dark at 60 °C for 48 h. The crude product was purified by column chromatography (hexanes) to give the cycloadduct **11c** (40.6 mg, 0.178 mmol, 82%) as a clear, colorless liquid. R_f = 0.58 (hexanes). GC (HP-1 column): retention time = 12.437 min. IR (neat): $\tilde{\nu}$ = 3128 (w), 3060 (s), 2972 (s), 2950 (s), 2876 (m), 1947 (w), 1878 (w), 1802 (w), 1752 (w), 1637 (s), 1598 (m), 1490 (s), 1448 (s), 1319 (s), 1293 (s), 1259 (s), 1222 (s), 1193 (s), 1125 (s), 1026 (m), 943 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.65 (dm, J = 7.4 Hz, 2 H), 7.39 (tm, J = 7.4 Hz, 2 H), 7.31 (tm, J = 7.4 Hz, 1 H), 6.25 (dd, J = 5.5, 2.9 Hz, 1 H), 6.21 (dd, J = 5.5, 2.9 Hz, 1 H), 2.76 (br. s, 1 H), 2.75 (br. s, 1 H), 2.71 (br. s, 1 H), 2.70 (br. s, 1 H), 1.50 (d, ^2J = 9.4 Hz, 1 H), 1.44 (dm, ^2J = 9.4 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 141.4, 136.6, 135.9, 132.0, 128.5, 128.1, 126.0, 125.6, 51.0, 43.7, 40.1, 39.5, 38.1 ppm. HRMS: calcd. for $C_{15}H_{13}Cl$ 228.0706, found 228.0701.

Cycloadduct 11d and Byproduct 12a (Table 3, Entry 8): According to the above general procedure (B) with norbornadiene (**5**, 110 μL, 1.02 mmol), alkynyl iodide **10d** (78.9 mg, 0.346 mmol), THF (0.70 mL), and Cp*RuCl(COD) (10.5 mg, 0.0276 mmol). The reaction mixture was stirred in the dark at 65 °C for 43 h. The crude product was purified by column chromatography (hexanes) to give the cycloadduct **11b** (45.0 mg, 0.141 mmol, 41%) as a colorless oil and the addition product **12a** (28.8 mg, 0.090 mmol, 26%).

11d: R_f = 0.42 (hexanes). IR (neat): $\tilde{\nu}$ = 3058 (m), 3020 (w), 2971 (s), 2947 (s), 2873 (w), 1482 (m), 1446 (m), 1319 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.76–7.78 (m, 2 H), 7.35–7.42 (m, 3 H), 6.22 (m, 2 H), 3.04 (br. d, J = 3.7 Hz, 1 H), 2.73–2.75 (m, 2 H), 2.55 (m, 1 H), 1.42 (m, 2 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 153.4, 136.6, 136.2, 133.0, 129.1, 128.7, 125.2, 88.4, 53.5, 50.3, 40.8, 39.7, 39.2 ppm. HRMS: calcd. for $C_{15}H_{13}I$ 320.0062, found 320.0069.

12a: R_f = 0.32 (hexanes). IR (neat): $\tilde{\nu}$ = 3163 (w), 3061 (s), 2984 (s), 2871 (m), 2203 (w), 1723 (m), 1665 (m), 1598 (s), 1490 (s), 1443 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.49–7.51 (m, 2 H), 7.29–7.33 (m, 3 H), 6.26 (dd, J = 5.6, 2.8 Hz, 1 H), 6.08 (dd, J = 5.6, 3.0 Hz, 1 H), 4.01 (dd, J = 7.5, 2.3 Hz, 1 H), 3.31 (br. s, 1 H), 3.08 (br. s, 1 H), 2.64 (dd, J = 7.5, 1.5 Hz, 1 H), 2.24 (d, J = 9.2 Hz, 1 H), 1.75 (dm, J = 9.2 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 137.8, 135.8, 131.5, 128.2, 127.9, 123.6, 94.5, 85.0, 54.3, 50.6, 45.3, 37.1, 32.1 ppm. HRMS: calcd. for $C_{15}H_{13}I$ 320.0062, found 320.0058.

Cycloadduct 11e (Table 5, Entry 3): According to the above general procedure (B) with norbornene **13** (288.4 mg, 3.06 mmol), alkynyl chloride **10c** (71.5 mg, 0.52 mmol), THF (1.6 mL), and Cp*RuCl(COD) (7.5 mg, 0.02 mmol). The reaction mixture was stirred in the dark at 65 °C for 140 h. The crude product was purified by column chromatography (hexanes) to give the cycloadduct **11e** (53.9 mg, 0.234 mmol, 45%) as a pale yellow oil. R_f = 0.59 (hexanes). IR (neat): $\tilde{\nu}$ = 2952 (m), 2870 (m), 1635 (m), 1490 (w), 1447 (m), 1315 (w), 1239 (w), 1261 (w), 1204 (m), 1124 (w), 957 (s), 919 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.59 (m, 2 H), 7.35 (m, 2 H), 7.27 (m, 1 H), 2.74 (dd, J = 12.0, 3.5 Hz, 2 H), 2.26 (br. s, 1 H), 2.20 (br. s, 1 H), 1.65–1.59 (m, 2 H), 1.41 (br. d, J = 10.5 Hz, 2 H), 1.17–1.12 (m, 2 H), 1.04 (dt, J = 10.5, 1.3 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 140.1, 132.4, 128.6, 128.1, 126.3, 121.0, 53.5, 46.3, 35.2, 33.0, 30.7, 28.2, 27.9 ppm. HRMS: calcd. for $C_{15}H_{15}Cl$ 230.0862, found 230.0868.

Cycloadduct 11f (Table 5, Entry 4): According to the above general procedure (B) with norbornene (**13**, 235.5 mg, 2.51 mmol), alkynyl bromide **8a** (73.9 mg, 0.41 mmol), THF (1.6 mL), and Cp*RuCl(COD) (8.4 mg, 0.02 mmol). The reaction mixture was

stirred in the dark at 65 °C for 140 h. The crude product was purified by column chromatography (hexanes) to give the cycloadduct **11f** (56.3 mg, 0.205 mmol, 50%) as a pale yellow oil. R_f = 0.52 (hexanes). IR (neat): $\tilde{\nu}$ = 2950 (s), 2870 (m), 1628 (s), 1489 (w), 1446 (w), 1314 (w), 1294 (w), 1255 (w), 1202 (w), 947 (m), 904 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.67 (d, J = 7.2 Hz, 2 H), 7.36 (br. t, J = 7.5 Hz, 2 H) 7.29 (br. t, J = 7.3 Hz, 1 H) 2.90 (d, J = 3.2 Hz, 1 H), 2.80 (d, J = 3.2 Hz, 1 H), 2.76 (br. s, 1 H) 2.17 (br. s, 1 H) 1.68–1.56 (m, 2 H), 1.41 (br. d, J = 10.5 Hz, 1 H), 1.69–1.14 (m, 2 H), 1.04 (d, J = 10.5 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 144.1, 132.5, 128.5, 128.4, 125.9, 109.7, 54.5, 49.0, 35.1, 33.4, 30.7, 27.9, 27.7 ppm. HRMS: calcd. for $C_{15}H_{15}Br$ 274.0357, found 274.0362.

Cycloadduct 11g (Table 5, Entry 5): According to the above general procedure (B) with oxabenzonorbornadiene **14** (44.0 mg, 0.31 mmol), alkynyl chloride **10c** (33.2 mg, 0.24 mmol), THF (0.8 mL), and Cp*RuCl(COD) (5.9 mg, 0.016 mmol). The reaction mixture was stirred in the dark at 65 °C for 48 h. The crude product was purified by column chromatography (10% EtOAc/hexanes) to give the cycloadduct **11g** (59.0 mg, 0.208 mmol, 87%) as a pale yellow powder. R_f = 0.49 (10% EtOAc/hexanes). IR (neat): $\tilde{\nu}$ = 3055 (w), 3025 (w), 2999 (w), 2953 (w), 1636 (w), 1490 (m), 1458 (m), 1447 (m), 1267 (s), 1221 (w), 1197 (m), 1116 (m), 1025 (w), 982 (m), 954 (s), 902 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.74 (d, J = 8.1 Hz, 2 H), 7.46 (t, J = 8.0 Hz, 2 H), 7.41–7.35 (m, 3 H), 7.26–7.24 (m, 2 H), 5.21 (s, 2 H), 3.11 (d, J = 3.5 Hz, 1 H), 3.05 (d, J = 3.5 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 144.6, 144.0, 140.0, 131.4, 128.5 (2), 126.93, 126.89, 126.1, 122.5, 119.9, 119.8, 76.1, 75.0, 52.0, 45.1 ppm. HRMS: calcd. for $C_{18}H_{13}ClO$ 280.0655, found 280.0650.

Cycloadduct 11h (Table 5, Entry 6): According to the above general procedure (B) with oxabenzonorbornadiene **14** (47.5 mg, 0.33 mmol), alkynyl bromide **8a** (41.8 mg, 0.23 mmol), THF (0.8 mL), and Cp*RuCl(COD) (4.2 mg, 0.011 mmol). The reaction mixture was stirred in the dark at 65 °C for 48 h. The crude product was purified by column chromatography (hexanes) to give the cycloadduct **11h** (52.0 mg, 0.161 mmol, 70%) as a pale yellow powder. R_f = 0.45 (10% EtOAc/hexanes). IR (neat): $\tilde{\nu}$ = 3054 (w), 3023 (w), 2997 (w), 2954 (m), 1731 (w), 1633 (w), 1597 (w), 1493 (m), 1464 (m), 1454 (m), 1262 (s), 1195 (m), 1173 (m), 1150 (w), 1024 (w), 982 (m), 942 (s), 901 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.78–7.76 (m, 2 H) 7.43–7.40 (m, 2 H), 7.37–7.30 (m, 3 H), 7.21–7.18 (m, 2 H), 5.16 (s, 1 H), 5.11 (s, 1 H), 3.18 (d, J = 3.5 Hz, 1 H), 3.04 (d, J = 3.5 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 144.4, 144.0, 143.7, 131.6, 128.8, 128.5, 128.97, 126.91, 125.7, 120.0, 119.98, 111.2, 76.0, 75.3, 53.0, 47.6 ppm. HRMS: calcd. for $C_{18}H_{13}BrO$ 324.0150, found 324.0154.

Cycloadduct 11i (Table 5, Entry 7): According to the above general procedure (B) with oxabenzonorbornadiene **15** (64.4 mg, 0.315 mmol), alkynyl chloride **10c** (37.4 mg, 0.275 mmol), THF (0.6 mL), and Cp*RuCl(COD) (8.0 mg, 0.021 mmol). The reaction mixture was stirred in the dark at 65 °C for 140 h. The crude product was purified by column chromatography (EtOAc/hexanes, 1:4) to give the cycloadduct **11i** (51.1 mg, 0.150 mmol, 55%) as a pale yellow powder. R_f = 0.44 (EtOAc/hexanes, 1:4). IR (neat): $\tilde{\nu}$ = 3001 (w), 2956 (w), 2908 (w), 2835 (w), 1637 (w), 1614 (w), 1500 (s), 1463 (w), 1443 (w), 1439 (w), 1401 (w), 1259 (s), 1221 (w), 1181 (w), 1146 (w), 1116 (w), 1083 (w), 1026 (w), 993 (m), 984 (w), 958 (w), 945 (w), 904 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.71 (d, J = 7.3 Hz, 2 H), 7.38 (m, 3 H), 6.70 (s, 2 H), 5.35 (s, 2 H), 3.85 (s, 3 H), 3.83 (s, 3 H), 3.10 (d, J = 3.5 Hz, 1 H), 3.04 (d, J = 3.5 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 147.40, 147.36, 139.8, 133.6, 133.0, 131.4, 128.5 (2), 126.1, 122.7, 111.6, 111.5, 74.3, 73.3, 56.1, 56.0, 51.5, 44.6 ppm. HRMS: calcd. for $C_{20}H_{17}ClO_3$ 340.0866, found 340.0861.

Cycloadduct 11j (Table 5, Entry 8): According to the above general procedure (B) with oxabenzonorbornadiene **15** (85.0 mg, 0.416 mmol), alkynyl bromide **8a** (64.5 mg, 0.358 mmol), THF (0.6 mL), and Cp*RuCl(COD) (8.6 mg, 0.023 mmol). The reaction mixture was stirred in the dark at 65 °C for 160 h. The crude product was purified by column chromatography (EtOAc/hexanes, 1:4) to give the cycloadduct **11j** (95.7 mg, 0.249 mmol, 70%) as a pale yellow powder. R_f = 0.49 (EtOAc/hexanes, 1:4). IR (neat): $\tilde{\nu}$ = 3079 (w), 3060 (w), 2994 (w), 2953 (w), 2907 (w), 2834 (w), 1499 (m), 1461 (w), 1439 (w), 1401 (w), 1311 (w), 1259 (m), 1218 (w), 1178 (w), 1148 (w), 1106 (w), 1025 (w), 989 (w), 952 (w), 936 (w), 902 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.79 (d, J = 7.1 Hz, 2 H), 7.41 (m, 3 H), 6.70 (d, J = 5.5 Hz, 2 H), 5.35 (s, 1 H), 5.31 (s, 1 H), 3.85 (s, 3 H), 3.83 (s, 3 H), 3.22 (d, J = 3.5 Hz, 1 H), 3.09 (d, J = 3.4 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 147.44, 147.40, 143.9, 133.4, 132.9, 131.6, 128.7, 128.5, 125.7, 111.6, 111.5, 111.3, 74.1, 73.5, 56.0, 55.7, 52.4, 47.0 ppm. HRMS: calcd. for $C_{20}H_{17}BrO_3$ 384.0361, found 384.0365.

Cycloadduct 11k (Table 5, Entry 9): According to the above general procedure (B) with oxabenzonorbornadiene **16** (100.6 mg, 0.33 mmol), alkynyl chloride **10c** (37.0 mg, 0.27 mmol), THF (0.8 mL), and Cp*RuCl(COD) (4.6 mg, 0.012 mmol). The reaction mixture was stirred in the dark at 65 °C for 48 h. The crude product was purified by column chromatography (10% EtOAc/hexanes) to give the cycloadduct **11k** (48.1 mg, 0.110 mmol, 41%) as a pale yellow powder. R_f = 0.58 (10% EtOAc/hexanes). IR (neat): $\tilde{\nu}$ = 3059 (w), 3025 (w), 2999 (w), 2960 (w), 1638 (m), 1599 (m), 1490 (m), 1446 (m), 1360 (m), 1319 (m), 1287 (w), 1269 (m), 1194 (w), 1174 (m), 1117 (w), 1088 (m), 988 (w), 955 (s), 910 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.65–7.63 (m, 2 H) 7.58 (s, 1 H), 7.55 (s, 1 H), 7.42–7.38 (m, 2 H), 7.33 (m, 1 H), 5.10–5.10 (m, 2 H), 3.05 (d, J = 3.5 Hz, 1 H), 2.98 (d, J = 3.5 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 146.2, 145.6, 139.9, 131.5, 129.3, 129.1, 126.5, 125.84, 125.75, 123.2 (2), 122.6, 16.2, 17.1, 51.9, 45.1 ppm. HRMS: calcd. for $C_{18}H_{11}Br_2ClO$ 435.8865, found 435.8860.

Cycloadduct 11l (Table 5, Entry 10): According to the above general procedure (B) with oxabenzonorbornadiene **16** (65.6 mg, 0.32 mmol), alkynyl bromide **8a** (38.5 mg, 0.28 mmol), THF (0.8 mL), and Cp*RuCl(COD) (6.9 mg, 0.018 mmol). The reaction mixture was stirred in the dark at 65 °C for 48 h. The crude product was purified by column chromatography (hexanes) to give the cycloadduct **11l** (77.4 mg, 0.16 mmol, 70%) as a pale yellow powder. R_f = 0.52 (10% EtOAc/hexanes). IR (neat): $\tilde{\nu}$ = 3024 (w), 2999 (w), 2959 (w), 2917 (w), 2849 (w), 1633 (w), 1597 (w), 1566 (w), 1489 (m), 1445 (m), 1359 (m), 1319 (m), 1286 (w), 1264 (m), 1172 (m), 1108 (w), 1087 (m), 988 (m), 945 (s), 910 (s) (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.72–7.70 (m, 2 H), 7.58 (s, 2 H), 7.56 (s, 1 H), 7.43–7.35 (m, 3 H), 510 (s, 1 H), 5.06 (s, 1 H), 3.16 (d, J = 3.5 Hz, 1 H), 3.03 (d, J = 3.5 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 146.0, 145.5, 144.0, 131.7, 129.5, 129.1, 126.1, 125.87, 125.80, 123.22, 123.16, 111.1, 76.0, 75.4, 52.7, 47.5 ppm. HRMS: calcd. for $C_{18}H_{11}Br_3O$ 479.8360, found 479.8355.

Cycloadduct 11m (Table 5, Entry 11): According to the above general procedure (B) with azabenzonorbornadiene **17** (46.1 mg, 0.268 mmol), alkynyl chloride **10c** (35.1 mg, 0.257 mmol), THF (0.6 mL), and Cp*RuCl(COD) (6.0 mg, 0.016 mmol). The reaction mixture was stirred in the dark at 65 °C for 120 h. The crude prod-

uct was purified by column chromatography (EtOAc/hexanes, 1:9) to give the cycloadduct **11m** (85.4 mg, 0.225 mmol, 88%, as a mixture of two conformers due to the two different orientations of the BOC group on the nitrogen atom) as a yellow oil. R_f = 0.30 (EtOAc/hexanes, 1:9). IR (neat): $\tilde{\nu}$ = 3377 (w), 3057 (w), 3026 (w), 2975 (w), 2930 (w), 1699 (s), 1634 (w), 1598 (w), 1530 (w), 1491 (w), 1477 (w), 1448 (w), 1390 (s), 1366 (m), 1290 (m), 1265 (w), 1232 (w), 1206 (m), 1166 (m), 1115 (w), 1090 (m), 1046 (w), 1026 (w), 954 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.69 (m, 2 H), 7.37 (m, 5 H), 7.20 (m, 2 H), 5.14 (m, 2 H), 2.93 (m, 2 H), 1.39 (s, 3 H), 1.02 (s, 6 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 153.8, 153.6, 144.0, 143.7, 143.6, 143.0, 141.5, 140.5, 131.9, 131.4, 128.7, 128.4, 126.8, 126.7, 126.6, 126.3, 126.1, 124.8, 120.3, 120.1, 79.7, 79.5, 60.2, 59.3, 58.7, 57.9, 52.8, 52.6, 45.7, 28.1, 27.7 ppm (two sets of ^{13}C signals were observed due to the two conformers of the two different orientations of the BOC group on the nitrogen atom). HRMS: calcd. for $C_{23}H_{22}ClNO_2$ 379.1339, found 379.1344.

Cycloadduct 11n (Table 5, Entry 12): According to the above general procedure (B) with azabenzonorbornadiene **17** (67.7 mg, 0.278 mmol), alkynyl bromide **8a** (40.9 mg, 0.226 mmol), THF (0.6 mL), and Cp*RuCl(COD) (6.3 mg, 0.017 mmol). The reaction mixture was stirred in the dark at 65 °C for 140 h. The crude product was purified by column chromatography (EtOAc/hexanes, 1:9) to give the cycloadduct **11n** (66.6 mg, 0.157 mmol, 70%, as a mixture of two conformers due to the two different orientations of the BOC group on the nitrogen atom) as a yellow oil. R_f = 0.21 (EtOAc/hexanes, 1:9). IR (neat): $\tilde{\nu}$ = 3380 (w), 3057 (w), 2975 (w), 2930 (w), 1698 (s), 1631 (w), 1597 (w), 1530 (w), 1490 (w), 1477 (w), 1460 (w), 1447 (w), 1390 (s), 1366 (m), 1289 (m), 1258 (w), 1230 (w), 1204 (w), 1166 (m), 1107 (w), 1090 (m), 1043 (w), 1025 (w), 958 (w), 941 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.76 (m, 2 H), 7.39 (m, 5 H), 7.20 (m, 2 H), 5.11 (m, 2 H), 3.00 (m, 2 H), 1.40 (s, 3 H), 1.03 (s, 6 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 153.7, 153.4, 144.8, 144.6, 144.2, 144.0, 143.9, 143.6, 143.0, 132.1, 129.0, 128.4, 126.8, 126.6, 126.0, 125.8, 120.5, 120.1, 113.6, 112.0, 79.8, 79.6, 60.2, 59.5, 58.6, 58.2, 54.1, 53.8, 48.1, 47.9, 28.2, 27.8 ppm (two sets of ^{13}C NMR signals were observed due to the two conformers of the two different orientations of the BOC group on the nitrogen atom). HRMS: calcd. for $C_{23}H_{22}BrNO_2$ 423.0834, found 423.0838.

Cycloadducts 19a and 20a (Table 6, Entry 1): According to the above general procedure (B) with C1-substituted oxabenzonorbornadiene **18** (1.5 equiv.), alkynyl chloride **10c** (22.4 mg, 0.165 mmol), THF (0.4 mL), and Cp*RuCl(COD) (5 mol-%). The reaction mixture was stirred in the dark at 65 °C for 48 h. The crude product was purified by column chromatography (10% EtOAc/hexanes) to give an inseparable mixture of regioisomers **19a** and **20a** (17.0 mg, 0.0503 mmol, 31%; **19a/20a** = 1.2:1, determined by ^1H NMR) as a pale orange powder. R_f = 0.30 (10% EtOAc/hexanes). IR (neat): $\tilde{\nu}$ = 3055 (m), 3026 (m), 3004 (m), 2953 (m), 2850 (m), 1763 (s), 1736 (s), 1638 (w), 1598 (w), 1577 (w), 1492 (m), 1457 (s), 1446 (s), 1438 (s), 1354 (s), 1329 (s), 1268 (s), 1214 (s), 1198 (s), 1183 (m), 1159 (m), 1107 (s), 1061 (m), 1021 (m), 963 (m), 927 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.74–7.72 (m, 1 H), 7.65–7.58 (m, 4 H), 7.42–7.31 (m, 7 H), 7.30–7.25 (m, 3 H), 5.64 (s, 0.7 H), 5.27 (s, 1 H), 3.82 (s, 2.2 H), 3.58 (s, 3 H), 3.46 (d, J = 3.4 Hz, 1 H), 3.08 (d, J = 3.4 Hz, 1 H), 2.78 (d, J = 6.4 Hz, 0.7 H), 2.29 (d, J = 6.4 Hz, 0.7 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 168.6, 168.5, 145.8, 144.0, 143.0, 142.3, 138.7, 135.5, 130.8, 128.7, 128.3, 128.1, 127.7, 127.3, 127.2, 126.81, 126.77, 126.13, 126.10, 126.0, 123.4, 120.2, 119.9, 119.8, 86.9, 83.6, 79.3, 75.1, 53.2, 52.5, 52.1, 48.1, 34.6, 28.7 ppm. HRMS (CI): calcd. for $C_{20}H_{15}ClO_3$ [M^+] 338.0710, found 338.0706. $C_{20}H_{15}ClO_3$ (338.79): calcd. C 70.91, H 4.46; found C 71.10, H 4.09.

Cycloadducts 19b and 20b (Table 6, Entry 2): According to the above general procedure (B) with C1-substituted oxabenzonorbornadiene **18** (100 mg, 0.495 mmol), alkynyl bromide **8a** (70.0 mg, 0.389 mmol), THF (0.8 mL), and Cp*RuCl(COD) (7.0 mg, 0.018 mmol). The reaction mixture was stirred in the dark at 65 °C for 48 h. The crude product was purified by column chromatography (EtOAc/hexanes, 1.5:8.5) to give the cycloadducts **19b** and **20b** as a mixture of regioisomer [**19b/20b** = 1.7:1, determined by GC (HP-1 column); retention time of major isomer = 31.581 min, retention time of minor isomer = 33.025 min].

19b: Fractional recrystalization of the above mixture from Et_2O/pentane (2:8) afforded a pure sample of cycloadduct **19b** as a white solid (36.2 mg, 0.094 mmol, 25%); R_f = 0.32 (EtOAc/hexanes, 2:8); m.p. 148–149 °C; assignment of structure based on 1D GOESY NMR experiments. IR (CH_2Cl_2): $\tilde{\nu}$ = 3070 (w), 2947 (w), 1761 (s), 1737 (s), 1621 (w), 1487 (m), 1449 (m), 1352 (m), 1309 (m), 1261 (m), 1199 (s), 1104 (m), 1065 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.75 (d, J = 6.9 Hz, 2 H), 7.55 (m, 1 H), 7.40 (m, 4 H), 7.27 (m, 2 H), 5.26 (s, 1 H), 4.00 (s, 3 H), 3.35 (d, J = 3.4 Hz, 1 H), 3.26 (d, J = 3.4 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 75 MHz): δ = 167.8, 144.5, 143.6, 142.1, 131.2, 129.2, 128.5, 127.7, 127.3, 125.9, 120.2, 120.0, 109.5, 83.3, 76.0, 54.9, 52.6, 49.0 ppm. HRMS (EI): calcd. for $C_{20}H_{15}BrO_3$ [M^+] 382.0205, found 382.0210. $C_{20}H_{15}BrO_3$ (383.24): calcd. C 62.68, H 3.95; found C 62.99, H 3.67.

20b: Purification of the mixture of cycloadducts by column chromatography (CH_2Cl_2) afforded a pure sample of cycloadduct **20b** as a pale yellow solid (21.6 mg, 0.056 mmol, 14%); R_f = 0.37 (EtOAc/hexanes, 2:8); m.p. 45–47 °C; assignment of structure based on 1D GOESY NMR experiments. ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.67 (m, 3 H), 7.37 (m, 4 H), 7.27 (m, 2 H), 5.22 (s, 1 H), 3.57 (d, J = 3.4 Hz, 1 H), 3.56 (s, 3 H), 3.12 (d, J = 3.4 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 75 MHz): δ = 168.6, 143.1, 142.9, 142.6, 131.2, 129.0, 128.3, 127.8, 127.3, 125.9, 120.4, 120.0, 112.2, 83.5, 75.5, 54.1, 52.2, 50.6 ppm. $C_{20}H_{15}BrO_3$ (383.24): calcd. C 62.68, H 3.95; found C 62.87, H 3.76.

Cycloadducts 19c and 20c (Table 6, Entry 3): According to the above general procedure (B) with C1-substituted oxabenzonorbornadiene **18** (1.5 equiv.), alkynyl iodide **10d** (35.8 mg, 0.158 mmol), THF (0.4 mL), and Cp*RuCl(COD) (5 mol-%). The reaction mixture was stirred in the dark at 65 °C for 48 h. The crude mixture was purified by column chromatography (EtOAc/hexanes, 1:9) to obtain **19c** and **20c** [**19b/20b** = 1.4:1, determined by GC (HP-1 column); retention time of major isomer = 34.733 min, retention time of minor isomer = 33.195 min] in a 41% combined yield.

Cycloadduct 19c: Obtained as a yellow solid (EtOAc/hexanes, 1:9, R_f = 0.20) (18.7 mg, 0.044 mmol, 27%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.83–7.80 (m, 2 H), 7.56–7.53 (m, 1 H), 7.45–7.36 (m, 5 H), 7.30–7.25 (m, 1 H), 5.25 (s, 1 H), 4.01 (s, 3 H), 3.40 (d, J = 3.4 Hz, 1 H), 3.31 (d, J = 3.4 Hz, 1 H) ppm. ^{13}C NMR (APT, CDCl3, 75 MHz): δ = 167.7, 151.7, 143.4, 142.1, 131.8, 129.4, 128.4, 127.7, 127.3, 125.0, 120.1, 120.0, 81.4, 76.0, 55.2, 52.6, 52.0 ppm. IR (NaCl): $\tilde{\nu}$ = 3055 (w), 3026 (w), 2995 (w), 2951 (w), 2921 (w), 2850 (w), 1762 (s), 1737 (s), 1489 (m), 1457 (m), 1446 (m), 1437 (m), 1353 (m), 1325 (m), 1289 (w), 1256 (m), 1211 (m), 1199 (m), 1160 (m), 1112 (m), 1068 (m), 1022 (w), 950 (m), 912 (m), 862 (w), 818 (w), 779 (m), 758 (m), 735 (m), 693 (m), 665 (w), 639 (m), 587 (w), 559 (w) cm^{-1}. Also characterized by 1D GOESY NMR experiments. $C_{20}H_{15}IO_3$ (430.24): calcd. C 55.83, H 3.51; found C 56.12, H 3.20.

Cycloadduct 20c: Obtained as a yellow solid (EtOAc/hexanes, 1:9, R_f = 0.28) (9.2 mg, 0.021 mmol, 14%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.75–7.72 (m, 2 H), 7.65–7.61 (m, 1 H), 7.43–7.34 (m, 5 H), 7.30–7.27 (m, 1 H), 5.11 (s, 1 H), 3.71 (d, J = 3.4 Hz, 1 H), 3.53 (s, 3 H), 3.08 (d, J = 3.4 Hz, 1 H), 1.54 (s, 3 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 75 MHz): δ = 168.6, 150.1, 1430 (2), 142.0, 131.7, 129.2, 128.3, 127.7, 127.3, 125.1, 120.4, 120.1, 85.0, 76.0, 54.9, 53.7, 52.1 ppm. IR (NaCl): $\tilde{\nu}$ = 3052 (w), 3027 (w), 2995 (w), 2949 (w), 2847 (w), 1763 (s), 1735 (s), 1489 (m), 1456 (m), 1437 (m), 1354 (m), 1328 (m), 1257 (m), 1211 (m), 1197 (m), 1178 (w), 1159 (m), 1109 (m), 1072 (m), 1054 (m), 1016 (w), 951 (m), 910 (w), 863 (w), 781 (m), 756 (s), 694 (m), 635 (m) cm^{-1}. Also characterized by 1D GOESY NMR experiments. $C_{20}H_{15}IO_3$ (430.24): calcd. C 55.83, H 3.51; found C 55.54, H 3.88.

Cycloaddition Between C1-Substituted Oxabenzonorbornadiene 18 and Alkynyl Chloride 10a (Table 6, Entry 4): According to the above general procedure (B) with C1-substituted oxabenzonorbornadiene **18** (1.5 equiv.), alkynyl chloride **10a** (44.9 mg, 0.339 mmol), THF (0.8 mL), and Cp*RuCl(COD) (5 mol-%). The reaction mixture was stirred in the dark at 65 °C for 48 h. The crude product was purified by column chromatography (10% EtOAc/hexanes) to give an inseparable mixture of regioisomers, cyclobutenes **19d** and **20d** [50.2 mg, 0.150 mmol, 44%; **19d/20d** = 61:1, determined by GC (HP-1 column): retention time of major isomer **19d** = 32.528 min, retention time of minor isomer **20d** = 33.033 min] as a yellow oil, together with an inseparable mixture of cyclotrimerization benzene derivatives **22a** and **23a** as a yellow oil (16.9 mg, 0.043 mmol, 38%).

Cycloadducts 19d and 20d: R_f = 0.30 (10% EtOAc/hexanes). IR (neat): $\tilde{\nu}$ = 3053 (w), 2982 (m), 2955 (m), 2925 (w), 2853 (w), 1765 (s), 1739 (s), 1716 (s), 1635 (m), 1458 (m), 1439 (m), 1316 (m), 1252 (m), 1202 (m), 1187 (m), 1135 (m), 1107 (m), 1063 (m), 1031 (m), 969 (m), 955 (m), 938 (m), 925 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.53–7.51 (m, 1 H), 7.36–7.34 (m, 1 H), 7.29–7.25 (m, 2 H), 5.29 (s, 1 H), 4.28 (q, J = 7.1 Hz, 2 H), 3.98 (s, 3 H), 3.23 (d, J = 3.4 Hz, 1 H), 3.07 (d, J = 3.4 Hz, 1 H), 1.36 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 167.4, 160.3, 143.4, 141.3, 138.8, 133.6, 128.0, 127.4, 120.3, 120.1, 82.7, 76.1, 60.9, 54.5, 52.8, 47.1, 14.2 ppm. HRMS (CI): calcd. for $C_{17}H_{15}ClO_5$ [M$^+$] 334.0608, found 334.0605. Also characterized by 1D GOESY NMR experiments. $C_{17}H_{15}ClO_5$ (334.76): calcd. C 61.00, H 4.52; found C 60.76, H 4.86.

Cyclotrimerization Benzene Derivatives 22a and 23a: R_f = 0.45 (EtOAc/hexanes, 1:4). IR (neat): $\tilde{\nu}$ = 2985 (s), 2940 (m), 2907 (m), 2874 (w), 1744 (br., s), 1563 (m), 1540 (m), 1466 (m), 1446 (m), 1417 (m), 1381 (m), 1361 (m), 1224 (br., m), 1106 (m), 1018 (br., s), 956 (w), 914 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.50–4.35 (m, 8 H), 1.42–1.34 (m, 12 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 163.6, 163.4, 163.0, 162.9, 147.7, 137.1, 135.1, 133.6, 133.0, 131.7, 130.0, 127.9, 63.00, 62.96, 62.86, 62.78, 14.0, 13.9 ppm. HRMS (CI): calcd. for $C_{15}H_{15}Cl_3O_6$ [M$^+$] 395.9934, found 395.9922. $C_{15}H_{15}Cl_3O_6$ (397.64): calcd. C 45.31, H 3.80; found C 45.68, H 3.51.

Cycloaddition Between C1-Substituted Oxabenzonorbornadiene 18 and Alkynyl Bromide 8i (Table 6, Entry 5): According to the above general procedure (B) with C1-substituted oxabenzonorbornadiene **18** (1.5 equiv.), alkynyl bromide **8i** (29.9 mg, 0.169 mmol), THF (0.4 mL), and Cp*RuCl(COD) (5 mol-%). The reaction mixture was stirred in the dark at 65 °C for 48 h. The crude product was purified by column chromatography (EtOAc/hexanes, 1:4) to give an inseparable mixture of regioisomers, cyclobutenes **19e** and **20e** [26.6 mg, 0.070 mmol, 42%; **19e/20e** = 18:1, determined by GC (HP-1 column): retention time of major isomer **19e** = 28.335 min, retention time of minor isomer **20e** = 26.684 min] an off-white solid, together with an inseparable mixture of cyclotrimerization benzene derivatives **22b** and **23b** as an orange oil (13.1 mg, 0.025 mmol, 44%).

Cycloadducts 19e and 20e: R_f = 0.36 (EtOAc/hexanes, 1:4). IR (neat): $\tilde{\nu}$ = 3650 (w), 3552 (w), 3412 (w), 3054 (m), 2983 (m), 2955 (m), 2905 (m), 1765 (s), 1739 (s), 1716 (s), 1627 (s), 1458 (s), 1439 (s), 1311 (s), 1200 (s), 1185 (s), 1130 (s), 1108 (s), 1063 (m), 1029 (m), 968 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.46–7.43 (m, 1 H), 7.29–7.26 (m, 1 H), 7.19–7.17 (m, 2 H), 5.20 (s, 1 H), 4.21 (q, J = 7.1 Hz, 2 H), 3.90 (s, 1 H), 3.20 (d, J = 3.3 Hz, 1 H), 3.07 (d, J = 3.3 Hz, 1 H), 1.28 (t, J = 7.1 Hz, 3 H); visible peaks for minor isomer: δ = 7.54 (m, 1 H), 5.11 (s, 1 H), 3.86 (s, 3 H), 3.15 (d, J = 3.5 Hz, 1 H), 2.99 (d, J = 3.6 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 75 MHz): δ = 167.3, 160.6, 143.3 (2), 141.4, 138.4, 128.0, 127.4, 120.4, 120.2, 83.0, 75.9, 60.9, 55.3, 52.7, 49.5, 14.2 ppm. Also characterized by 1D GOESY NMR experiments. $C_{17}H_{15}BrO_5$ (379.21): calcd. C 53.85, H 3.99; found C 53.48, H 4.36.

Cyclotrimerization Benzene Derivatives 22b and 23b: R_f = 0.50 (EtOAc/hexanes, 1:4). IR (neat): $\tilde{\nu}$ = 2984 (m), 2939 (w), 2905 (w), 1739 (br., s), 1551 (m), 1524 (w), 1466 (m), 1445 (m), 1405 (m), 1384 (m), 1375 (m), 1353 (w), 1335 (w), 1290 (br., s), 1221 (br., s), 1179 (m), 1157 (m), 1092 (m), 1017 (s), 946 (w) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.49–4.33 (m, 8 H), 1.65–1.24 (m, 12 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 164.6, 164.5, 164.3, 164.2, 141.4, 138.3, 137.3, 134.4, 125.5, 123.0, 117.5, 116.3, 62.9, 62.84, 62.78, 13.8 ppm. $C_{15}H_{15}Br_3O_6$ (530.99): calcd. C 33.93, H 2.85; found C 33.60, H 3.03.

Cycloadducts 19f and 20f (Table 6, Entry 6): According to the above general procedure (B) with C1-substituted oxabenzonorbornadiene **18** (1.5 equiv.), alkynyl iodide **10b** (35.5 mg, 0.158 mmol), THF (0.4 mL), and Cp*RuCl(COD) (5 mol-%). The reaction mixture was stirred in the dark at 65 °C for 48 h. The crude product was purified by column chromatography (EtOAc/hexanes, 1:4) to give an inseparable mixture of regioisomers **19f** and **20f** [41.1 mg, 0.101 mmol, 60%; **19f/20f** = 10:1, determined by GC (HP-1 column): retention time of major isomer **19f** = 30.040 min, retention time of minor isomer **20f** = 29.698 min] as a yellow oil. R_f = 0.35 (EtOAc/hexanes, 1:4). IR (neat): $\tilde{\nu}$ = 3072 (m), 3052 (m), 3983 (m), 2955 (m), 2903 (w), 2851 (w), 2256 (m), 1716 (s), 1611 (s), 1444 (s), 1354 (m), 1275 (m), 1201 (m), 1124 (m), 1107 (m), 1065 (m), 1049 (m), 1029 (m), 967 (m), 951 (m), 911 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.54–7.52 (m, 1 H), 7.36–7.34 (m, 1 H), 7.30–7.24 (m, 2 H), 5.29 (s, 1 H), 4.30 (q, J = 7.1 Hz, 2 H), 3.28 (m, 2 H), 1.38 (t, J = 7.1 Hz, 3 H); visible peaks for minor isomer δ = 5.11 (s, 1 H), 3.95 (s, 3 H), 3.51 (d, J = 3.2 Hz, 1 H), 3.06 (d, J = 3.2 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 167.0, 160.9, 146.2, 142.9, 141.3, 127.9, 127.3, 120.3, 120.0, 102.3, 83.1, 75.3, 60.7, 55.5, 52.5, 52.3, 14.1; visible peaks for minor isomer: δ = 127.8, 127.3, 120.6, 75.2, 53.7 ppm. HRMS (CI): calcd. for $C_{17}H_{15}IO_5$ [M$^+$] 425.9964, found 425.9950. Also characterized by 1D GOESY NMR experiments. $C_{17}H_{15}IO_5$ (426.21): calcd. C 47.91, H 3.55; found C 47.57, H 3.89.

Cycloadducts 19g and 20g (Table 6, Entry 7): According to the above general procedure (B) with C1-substituted oxabenzonorbornadiene **18** (1.5 equiv.), alkynyl bromide **8j** (45.3 mg, 0.175 mmol), THF (0.4 mL), and Cp*RuCl(COD) (5 mol-%). The reaction mixture was stirred in the dark at 65 °C for 48 h. The crude product was purified by column chromatography (EtOAc/hexanes, 3:7) to give **19g** (16.8 mg, 0.036 mmol, 21%; **19g/20g** = >99:1, no minor regioisomer can be detected by 400 MHz ^{1}H NMR) as a yellow

solid. R_f = 0.17 (EtOAc/hexanes, 1:4). IR (neat): $\tilde{\nu}$ = 3055 (m), 3009 (m), 2955 (m), 2925 (m), 2855 (m), 1763 (s), 1739 (s), 1594 (s), 1493 (w), 1458 (m), 1439 (m), 1402 (w), 1323 (s), 1268 (w), 1236 (w), 1202 (m), 1156 (s), 1108 (m), 1092 (m), 1079 (m), 963 (m), 923 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.85 (d, J = 8.3 Hz, 2 H), 7.37–7.32 (m, 3 H), 7.25–7.15 (m, 3 H), 4.98 (s, 1 H), 3.87 (s, 3 H), 3.21–3.19 (m, 2 H), 2.39 (s, 3 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 166.8, 145.6, 144.1, 142.4, 141.1, 136.1, 130.2, 128.6 (2), 127.7, 126.6, 120.5, 120.0, 83.3, 75.5, 55.0, 52.8, 51.0, 21.8 ppm. HRMS (ESI): calcd. for $C_{21}H_{17}BrO_5S$ [M + NH_4]$^+$ 478.0324, found 478.0313. $C_{21}H_{17}BrO_5S$ (461.33): calcd. C 54.68, H 3.71; found C 54.31, H 3.89.

Isomerization of C1-Substituted Oxabenzonorbornadiene 18 (Table 6, Entries 1–7 and Scheme 4): According to the above general procedure (B) with C1-substituted oxabenzonorbornadiene **18** (1.5 equiv.), various alknyl halides (Table 6) in THF, and Cp*RuCl(COD) (5 mol-%). The reaction mixture was stirred in the dark at 65 °C for 48 h. Apart from the [2+2] cycloadducts, the naphthols **21a** and **21b** were obtained as an inseparable mixture of regioisomers as a white solid in 10–56%, **21a/21b** = 7:1, determined by ^1H NMR spectroscopy of the crude product.

Naphthols 21a and 21b: R_f = 0.60 (EtOAc/hexanes, 1:9). IR (neat): $\tilde{\nu}$ = 3305 (w), 3053 (m), 3008 (m), 2955 (m), 2934 (m), 2853 (w), 1715 (m), 1662 (s), 1637 (s), 1599 (m), 1578 (m), 1506 (m), 1463 (m), 1439 (s), 1409 (m), 1368 (m), 1340 (s), 1273 (s), 1257 (s), 1194 (m), 1156 (m), 1091 (m), 992 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 11.98 (s, 1 H), 8.41 (d, J = 8.1 Hz, 1 H), 7.76 (d, J = 8.5 Hz, 2 H), 7.62–7.49 (m, 2 H), 7.28 (d, J = 9.0 Hz, 1 H), 3.99 (s, 3 H) ppm; visible peaks of minor isomer: δ = 8.91 (d, J = 8.4 Hz, 1 H), 8.18 (d, J = 7.2 Hz, 1 H), 8.02 (d, J = 7.8 Hz, 1 H), 7.88 (d, J = 7.8 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 171.4, 160.9, 137.2 (2), 129.4, 127.4, 125.7, 124.2, 123.9, 118.6, 105.6, 52.3 ppm. These are known compounds, and the spectroscopic data are identical to those reported in the literature.[35]

Functionalization of the Cycloadduct 9a

Lithium/Halide Exchange of 9a Followed by Trapping with Methyl Iodide To Give Cyclobutene 7b (Scheme 6): A solution of *tert*-butyllithium in pentane (1.7 M, 0.28 mL, 0.48 mmol) was added to a solution of **9a** (52.2 mg, 0.191 mmol) in THF (0.50 mL) at –70 °C under N_2 over 5 min. The reaction mixture was stirred for 30 min, and dry methyl iodide (40 μL, 0.64 mmol) was then slowly added. After stirring at –70 °C for 45 min, the reaction mixture was warmed to 25 °C for 30 min. The reaction was quenched with water and the mixture extracted 3 times with diethyl ether. The organic layers were combined, washed with brine, dried with magnesium sulfate, and concentrated by rotary evaporation. The crude product was purified by column chromatography to give **7b** (32.1 mg, 0.155 mmol, 81%) as a pale yellow oil.

Cyclobutene 7b: R_f = 0.63 (hexanes). GC (HP-1 column): retention time = 11.437 min. IR (neat): $\tilde{\nu}$ = 3062 (m), 2964 (s), 2929 (s), 2854 (w), 1715 (m), 1686 (m), 1603 (m), 1499 (m), 1447 (s), 1370 (m), 1322 (s), 1220 (w), 1071 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.40 (d, J = 7.7 Hz, 2 H), 7.34 (t, J = 7.7 Hz, 2 H), 7.20 (t, J = 7.7 Hz, 1 H), 6.16 (m_{ABX}, 2 H), 2.65 (s, 1 H), 2.55 (br. s, 1 H), 2.53 (s, 1 H), 2.27 (br. s, 1 H), 2.01 (s, 3 H), 1.37 (d, J = 8.8 Hz, 1 H), 1.27 (d, J = 8.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 141.3, 139.7, 135.9, 135.7, 135.3, 128.4, 126.5, 125.7, 45.7, 42.7, 40.0, 39.2, 38.1, 14.2 ppm. HRMS: calcd. for $C_{16}H_{16}$ 208.1252, found 208.1258.

Lithium/Halide Exchange of 9a Followed by Trapping with Cholotrimethylsilane To Give Cyclobutene 7c (Scheme 6): A solution of *tert*-butyllithium in pentane (1.7 M, 0.55 mL, 0.94 mmol) was added to a solution of **9a** (101.6 mg, 0.372 mmol) in THF (2 mL) at –70 °C under N_2 over 5 min. The reaction mixture was stirred for 30 min, and chlorotrimethylsilane (0.15 mL, 1.18 mmol) was then slowly added. After stirring at –70 °C for 45 min, the reaction mixture was warmed to 25 °C for 30 min. The reaction was quenched with water and the mixture extracted 3 times with diethyl ether. The organic layers were combined, washed with brine, dried with magnesium sulfate, and concentrated by rotary evaporation. The crude product was purified by column chromatography to give **7c** (86.2 mg, 0.324 mmol, 87%) as a pale yellow oil.

Cyclobutene 7c: R_f = 0.47 (hexanes). IR (neat): $\tilde{\nu}$ = 3125 (w), 3058 (m), 2964 (s), 2923 (s), 2870 (w), 1249 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.34 (m, 2 H), 7.26 (m, 2 H), 7.17 (m, 1 H), 6.07 (m, 2 H), 2.64 (br. d, J = 3.7 Hz, 1 H), 2.51 (br. s, 1 H), 2.41 (br. s, 1 H), 2.20 (br. d, J = 3.6 Hz, 1 H), 1.31 (d, J = 8.9 Hz, 1 H), 1.15 (d, J = 8.9 Hz, 1 H), 0.14 (s, 9 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 158.5, 166.4, 135.8, 135.7, 135.0, 128.3, 127.6, 125.9, 45.2, 43.1, 39.8, 39.7, 38.4, –0.9 ppm. HRMS: calcd. for $C_{18}H_{22}Si$ 266.1491, found 266.1484. $C_{18}H_{22}Si$ (266.46): calcd. C 81.14, H 8.32; found C 81.01, H 8.40.

Lithium/Halide Exchange of 9a Followed by Trapping with Methanol To Give Cyclobutene 7e (Scheme 6): A solution of *tert*-butyllithium in pentane (1.7 M, 0.28 mL, 0.48 mmol) was added to a solution of **9a** (51.3 mg, 0.188 mmol) in THF (0.5 mL) at –70 °C under N_2 over 5 min. The reaction mixture was stirred for 30 min, and dry methanol (23 μL, 0.57 mmol) was then slowly added. After stirring at –70 °C for 45 min, the reaction mixture was warmed to 25 °C for 30 min. The reaction was quenched with water and the mixture extracted 3 times with diethyl ether. The organic layers were combined, washed with brine, dried with magnesium sulfate, and concentrated by rotary evaporation. The crude product was purified by column chromatography to give **7e** (17.1 mg, 0.0901 mmol, 48%) as a pale yellow oil. This is a known compound, and the spectroscopic data are identical to those reported in the literature.[36]

Suzuki Coupling Between 9a and Phenylboronic Acid To Give Cyclobutene 7d (Scheme 6): A mixture of **9a** (52.8 mg, 0.193 mmol), phenylboronic acid (44.7 mg, 0.367 mmol), tris(dibenzylideneacetone)dipalladium(0) (12.1 mg, 0.0132 mmol), cesium fluoride (125.1 mg, 0.905 mmol), and tris(*tert*-butyl)phosphane (10% in hexane, 60 μL, 0.020 mmol) in deoxygenated THF (0.4 mL) was prepared in an oven-dried screw-cap vial under argon. The reaction mixture was stirred at 25 °C for 24 h. The crude product was purified by column chromatography (hexanes) to give **7d** (39.3 mg, 0.145 mmol, 75%) ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.60 (d, J = 7.2 Hz, 4 H), 7.34–7.38 (m, 4 H), 7.26–7.30 (m, 2 H), 6.24 (br. s, 2 H), 2.75 (br. s, 2 H), 2.70 (br. s, 2 H), 1.60 (br. d, J = 9.0 Hz, 1 H), 1.37 (br. d, J = 9.0 Hz, 1 H) ppm. This is a known compound, and the spectroscopic data are identical to those reported in the literature.[37]

Sonogashira Coupling Between 9a and Phenylacetylene To Give Cyclobutene 24 (Scheme 6): A mixture of **9a** (29.4 mg, 0.110 mmol), tetrakis(triphenylphosphane)palladium (6.3 mg, 0.0055 mmol), triethylamine (15 μL, 0.11 mmol), copper iodide (2.1 mg, 0.011 mmol), phenylacetylene (12 μL, 0.11 mmol) and deoxygenated THF (0.60 mL) was prepared in an oven-dried screw-cap vial under argon. The reaction mixture was stirred at 65 °C for 24 h. The crude product was purified by column chromatography (hexanes) to give **24** (20.4 mg, 0.0692 mmol, 64%) as a white solid.

Cyclobutene 24: M.p. 56–57 °C. R_f = 0.48 (hexanes). IR (neat): $\tilde{\nu}$ = 3058 (s), 3029 (m), 2969 (s), 2940 (s), 2874 (w), 1949 (w), 1880 (w), 1486 (s), 1447 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.77 (d,

J = 7.1 Hz, 2 H), 7.52–7.55 (m, 2 H), 7.29–7.42 (m, 6 H), 6.20–6.25 (m, 2 H), 2.76 (br. s, 2 H), 2.74 (br. d, *J* = 3.9 Hz, 1 H), 2.63 (br. d, *J* = 3.8 Hz, 1 H), 1.53 (br. d, *J* = 9.1 Hz, 1 H), 1.39 (br. d, *J* = 9.1 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 150.9, 136.1, 133.9, 131.6, 128.5, 128.4, 128.3, 125.8, 123.4, 121.6, 96.2, 85.3, 46.1, 43.7, 40.2, 39.6, 38.9 ppm. HRMS: calcd. for $C_{23}H_{18}$ 294.1409, found 294.1418. $C_{23}H_{18}$ (294.40): calcd. C 93.84, H 6.16; found C 93.62, H 6.30.

Supporting Information (see footnote on the first page of this article): ^1H and ^{13}C NMR spectra of all new compounds that do not have elemental analysis.

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