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Ruthenium-Catalyzed [2 + 2] Cycloadditions between Norbornene and Propargylic Alcohols or Their Derivatives

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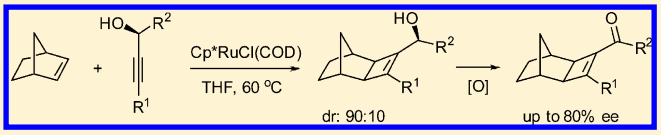
Supporting Information

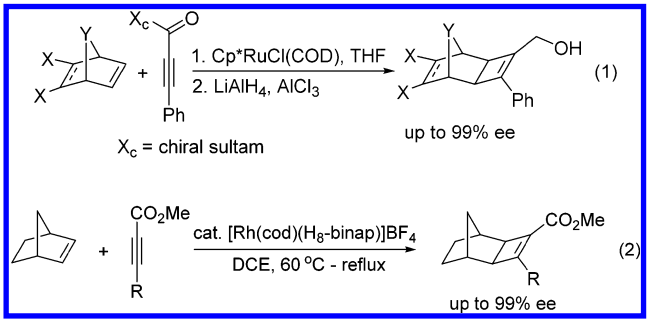
ABSTRACT: Diastereoselective ruthenium-catalyzed [2 + 2] cycloadditions of norbornene and propargylic alcohols or their derivatives were investigated. The cycloadditions were found to be highly stereoselective, giving exo cycloadducts in moderate to excellent yields with diastereoselectivities up to 92:8. When a chiral propargylic alcohol was used in the cycloaddition, up to 80% ee of the [2 + 2] cycloadducts was observed after oxidation of the alcohol.



INTRODUCTION

The development of ruthenium-catalyzed chemical processes has become an emerging field over the past decade.[1−4] With their wide range of oxidation states (from −2 to +8) and several coordination geometries, ruthenium catalysts can form a variety of intermediates such as (π-allyl)ruthenium,[5] ruthenium−carbene,[6] and ruthenacycle species.[7] Among various ruthenium complexes, CpRu(COD)Cl and Cp*Ru(COD)Cl have been found to be the catalysts of choice in many reactions such as [2 + 2 + 2] cycloadditions,[8−10] conjugate additions,[11] bis-Diels−Alder cycloadditions,[12] Alder-ene reactions,[13,14] cross-benzannulations,[15] and many others.[1,2] We and other groups have been largely involved in the preparation of cyclobutene rings via ruthenium-catalyzed [2 + 2] cycloadditions.[16−28]

Although asymmetric versions of transition-metal-catalyzed cycloaddition reactions such as [4 + 2],[29] [2 + 2 + 1],[30,31] [2 + 2 + 2],[32,33] and [4 + 2 + 2][34] have been recognized, to the best of our knowledge, very few studies on the asymmetric transition-metal-catalyzed [2 + 2] cycloadditions between an alkene and an alkyne have been reported in the literature. 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 sultam auxiliary, achieving excellent levels of asymmetric induction after recovery of the chiral auxiliary (eq 1).[35] More recently, rhodium-catalyzed enantioselective [2 + 2] cycloadditions of alkynyl esters and norbornene derivatives have been reported, demonstrating excellent enantioselectivity using a chiral rhodium catalyst (eq 2).[36]



In our preliminary communication[19] we reported a diastereoselective ruthenium-catalyzed [2 + 2] cycloaddition between bicyclic alkenes and chiral alkynes **2a−f** (Table 1). In this full paper, we have identified the previously undetermined structures of the major diastereomers, and have expanded our investigation to the effects of propargylic and acetylenic substituents on the diastereoselectivity of cycloaddition (Tables 2 and 3). The use of homopropargylic alcohols as the alkyne partner in the Ru-catalyzed cycloaddition has also been demonstrated (Table 4).

RESULTS AND DISCUSSION

Our initial trials of Ru-catalyzed [2 + 2] cycloaddition between norbornene **1** and chiral propargylic alcohol **2f** or its derivatives **2a−e** are summarized in Table 1. The chiral alkynes **2a−f** were synthesized from the common precursor (*S*)-(−)-3-butyn-2-ol ((*S*)-**3**), which was commercially available in an optically pure form (Scheme 1).

All cycloadditions were highly stereoselective, providing only exo cycloadducts **4**/**5** with yields from 33% to 71%. However, while in our preliminary communication we assumed that chiral alkynes **2a−f** all gave the same major diastereomers upon cycloaddition,[19] further investigation has shown that this is in fact not the case. In order to identify the structure of each major diastereomer unambiguously by X-ray diffraction analysis, we needed to find a pair of diastereomeric cycloadducts that were separable and crystalline. After numerous trials, we found that, when benzonorbornene **6** was reacted with the chiral propargylic alcohol **2f** under the cycloaddition conditions (Scheme 2), the diastereomeric cycloadducts **7** and **8** could be subsequently esterified with *p*-nitrobenzoyl chloride in pyridine to yield a

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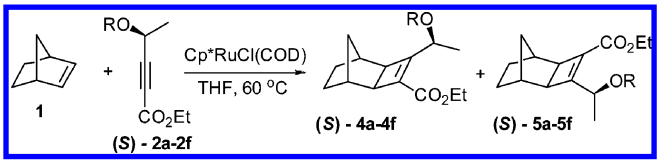
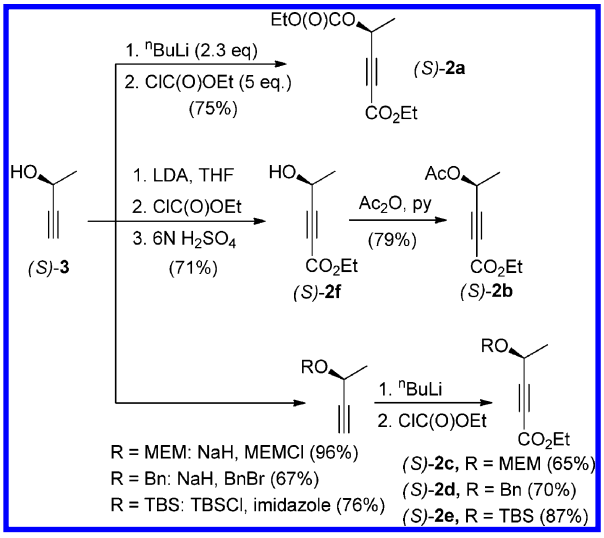
Table 1. Ru-Catalyzed [2 + 2] Cycloadditions between Norbornene 1 and Chiral Alkynes 2a−f



entry	alkyne	OR	time (h)	yield[a] (%)	dr[b] (4:5)
1	(*S*)-**2a**	OC(O)OEt	48	35	40:60
2	(*S*)-**2b**	OAc	62	33	40:60
3	(*S*)-**2c**	OMEM	72	45	42:58
4	(*S*)-**2d**	OBn	150	47	29:71
5	(*S*)-**2e**	OTBS	43	65	32:68
6	(*S*)-**2f**	OH	72	71	81:19

[a]Isolated yields after column chromatography. [b]Diastereomeric ratios (dr) were determined by GC and/or ^{1}H NMR (400 MHz).

Scheme 1. Synthesis of Chiral Alkynes 2a−f



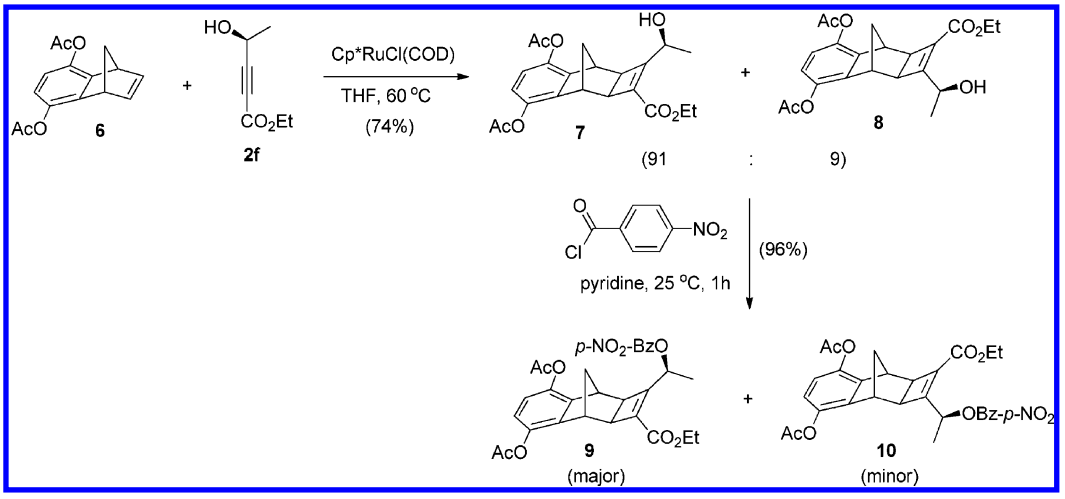
separable mixture of diastereomeric products **9** and **10**. Fractional recrystallization in Et_2O/hexanes provided the major diastereomer **9**. Suitable crystals were then grown from Et_2O/hexanes, and the structure of **9** was confirmed.[37]

Assuming that norbornene **1** and benzonorbornene **6** give similar major diastereomers in the Ru-catalyzed cycloaddition, the major diastereomer resulting from cycloaddition between norbornene **1** with chiral propargylic alcohol (*S*)-**2f** would be cycloadduct **4f** (Table 1, entry 6; **4f**:**5f** = 81:19). While the structure of the major diastereomer obtained from propargylic alcohol **2f** had been determined, NMR studies of the major diastereomers obtained from alkynes **2a−e** provided surprising results. A comparison of the ^{1}H NMR spectrum of the diastereomeric cycloadducts **4b**/**5b** (entry 2) with that of the same products obtained through a different route of cycloaddition with **2f** followed by acetylation demonstrates this (Scheme 3).

On the basis of the structures of the major diastereomer **9** (Scheme 2) and **4f** (Table 1, entry 6), the quartet between 5.7 and 5.8 ppm can be assigned to H^b while the quartet between 5.8 and 5.9 ppm is assigned to H^a. From the reversal in relative integration of these quartets, it is clear that the major diastereomer from the cycloaddition with alkyne **2b** is the opposite of that obtained from the cycloaddition with alkyne **2f**. Similar results were observed when the 81:19 mixture of diastereomeric cycloadducts **4f** and **5f** (Table 1, entry 6) was converted to **4a**/**5a**, **4c**/**5c**, **4d**/**5d**, or **4e**/**5e** and their NMR spectra were compared. Cycloaddition with alkynes **2a−e** in all cases gave the major diastereomer opposite of that formed via cycloaddition with alkyne **2f**. This suggests that a different mode of asymmetric induction is at play with propargylic alcohols. A plausible explanation for the difference in observed diastereoselectivity could invoke intramolecular hydrogen bonding (Figure 1). It has been reported that the chloride of M−Cl (M = metal) can act as a good hydrogen acceptor.[38] Recent computational studies have also suggested that such interactions are indeed present at every stage of Ru-catalyzed [2 + 2] cycloaddition of propargylic alcohols.[39] Therefore, the diastereoselectivity is thought to arise from a rigid ruthenium complex in which the metal interacts with the hydroxyl group of the alkyne via intramolecular hydrogen bonding.

To prove that the diastereoselectivities arise from the asymmetric induction of the chiral propargylic alcohol in the cycloadditions (and are not due to racemization of the chiral alcohol by the metal catalyst), the diastereomeric cycloadducts **4f**/**5f** were oxidized and the enantiomeric excess (ee) of the products was measured and compared to the diastereomeric ratio

Scheme 2. Structural Determination of the Major Diastereomer



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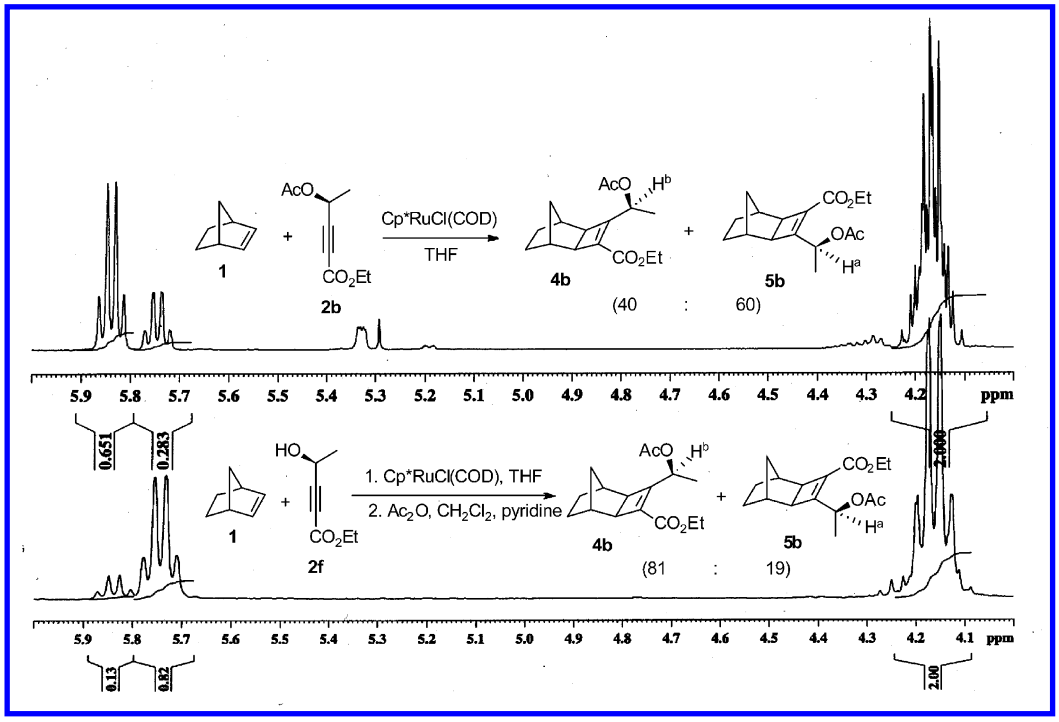
Scheme 3. Partial ^{1}H NMR Spectra of the Diastereomeric Cycloadducts 4b/5b



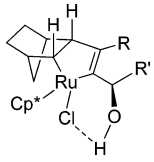


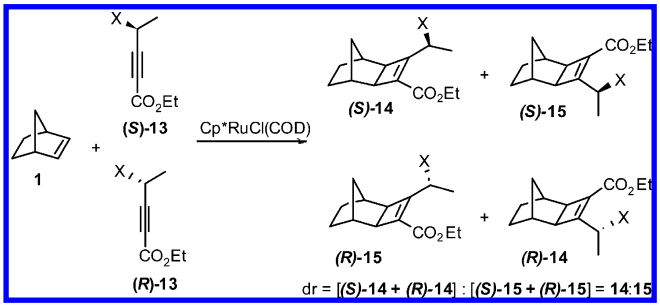
Figure 1. Possible intramolecular hydrogen bonding.

(dr) of the cycloadducts (Scheme 4). The diastereomeric ratio for the cycloadducts **4f**/**5f** was found to be identical with the enantiomeric ratio of products **11f**/**12f**; therefore, the diastereoselectivities must arise from asymmetric induction of the chiral propargylic alcohol in the cycloadditions.

It should be noted, however, that although only chiral alkynes were used in the above studies, identical diastereomeric ratios are to be expected from the use of racemic alkynes. For instance, while pure (*S*)-**13** affords compounds (*S*)-**14** and (*S*)-**15**, its enantiomer (*R*)-**13** would simply furnish the respective cycloadducts of opposite absolute stereochemistry, (*R*)-**14** and (*R*)-**15** (Scheme 5). Thus, although the chiral substituent helps to define the stereochemistry of the cycloadduct, the absolute stereochemistry of the alkyne does not affect the overall diastereomeric ratio. As such, subsequent studies were performed on racemic alkynes.

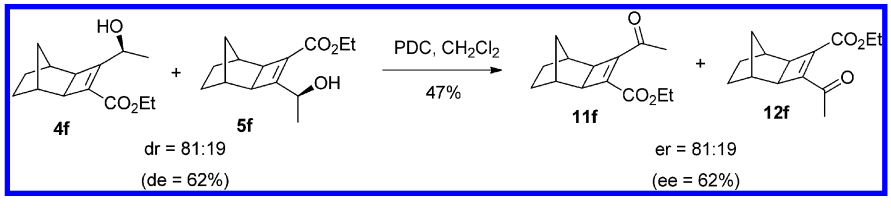
In order to investigate the effects of various propargylic substituents on the diastereoselectivity of cycloaddition, alkynes **16a**–**j** were prepared (Scheme 6). Protection of 3-butyn-2-ol

Scheme 5. Cycloaddition between Norbornene and a Racemic Alkyne



(**17**) followed by deprotonation with *n*-BuLi and trapping with paraformaldehyde, acetone, or di-*tert*-butyl dicarbonate and subsequent removal of the protecting group furnished various acetylenic substituent groups, including CH_2OH (**16a**), C-$(CH_3)_2OH$ (**16b**), and *tert*-butyl ester (**16c**). Bromination of **17** with NBS and $AgNO_3$ in acetone afforded propargylic alcohol **16d** with an acetylenic Br group, and deprotonation of terminal alkynes 1-hexyne (**18e**), 1-octyne (**18f**), and phenylacetylene (**18g**) afforded the corresponding propargylic alcohols with R^1 groups *n*-butyl (**16e**), *n*-hexyl (**16f**), and phenyl (**16g**). R^2 functionalized alcohols **16h**–**j** were similarly prepared by trapping the deprotonated ethyl propiolate (**19**) with the corresponding aldehyde. The effect of R^1 substituent on

Scheme 4. Comparison of dr Values of the Cycloadducts and er Values of the Oxidized Cycloadducts



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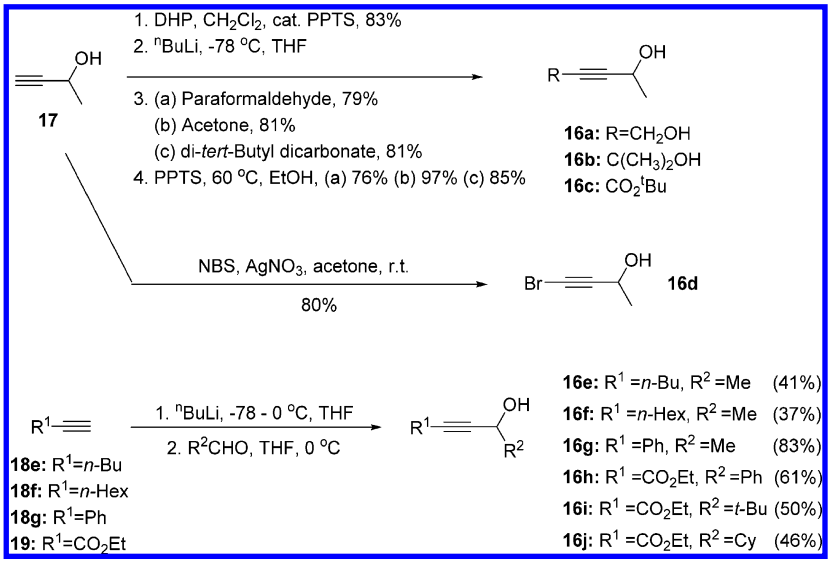
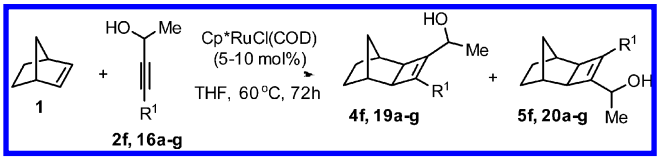
Scheme 6. Synthesis of Propargylic Alcohols 16a–j



diastereoselectivity was then assessed by reacting propargylic alcohols **16a–g** with norbornene **1** (Table 2).

Table 2. Effect of R^1 Substituent on Ru-Catalyzed [2 + 2] Cycloadditions between Norbornene and Propargylic Alcohols



entry	alcohol	R^1	yield[a] (%)	dr[b]
1	**2f**	COOEt	71	81:19
2	**16c**	COO-*t*-Bu	74	78:22
3	**16g**	Ph	57	64:36
4	**16e**	*n*-Bu	88	82:18
5	**16f**	*n*-Hex	44	77:23
6	**16a**	CH_2OH	61	55:45[c]
7	**16b**	$C(CH_3)_2OH$	56	50:50[c]
8	**16d**	Br	0[d]	N.A.

[a]Isolated yields after column chromatography. [b]Determined by GC and/or ^{1}H NMR (400 MHz). [c]Determined by GC from the acetylated products. [d]Full consumption of starting material determined by TLC; inseparable mixture of products.

Relative to alcohol **2f** (Table 2, entry 1), the diastereoselectivity was generally lower for the R^1 derivatized species. A small decrease in the diastereomeric ratio was observed when a bulky *tert*-butyl ester was present at the acetylenic position of alcohol **16c** (entry 2). The presence of a phenyl group in alcohol **16g** caused a sharp decrease in both diastereomeric ratio and yield (entry 3). Of the alcohols **16e,f** containing linear acetylenic alkyl groups, both a higher yield and diastereomeric ratio were observed for the *n*-butyl derivative (entries 4 and 5). Primary and tertiary alcohols of the diols **16a,b** had essentially no effect on diastereoselectivity, and the yields were moderate (entries 6 and 7). Finally, although thin-layer chromatography (TLC) indicated full consumption of starting material for bromide **16d**, the corresponding cycloadduct could not be isolated since an inseparable complicated mixture of products resulted (entry 8).

The effect of R^2 substituent on cycloaddition was then assessed (Table 3). Much to our delight, a significant improvement in

Table 3. Effect of Varying R^2 Substituent on Ru-Catalyzed [2 + 2] Cycloadditions between Norbornene and Various Propargylic Alcohols

entry	alcohol	R^2	yield[a] (%)	dr[b]
1	**2f**	Me	71	81:19
2	**16h**	Ph	74	90:10
3	**16i**	*t*-Bu	75	92:8
4	**16j**	Cy	98	88:12

[a]Isolated yields after column chromatography. [b]Diastereomeric ratios (dr) were determined by GC and/or ^{1}H NMR (400 MHz).

diastereoselectivity was observed when a bulkier R^2 substituent was present on the alkyne, relative to propargylic alcohol **2f**. While diastereomeric ratios were similar for all R^2 derivatized cycloadducts, the *t*-Bu derivative gave the highest diastereoselectivity of 92:8 for **19**:**20** (entry 3). Moreover, cycloadducts **20h–j** were obtained in good to excellent yields, with the cyclohexyl adduct **20j** obtained in 98% isolated yield, the highest achieved in our studies thus far.

Next an asymmetric version of the cycloaddition was performed using the chiral propargylic alcohol (*R*)-**21**, prepared from its enantiomerically pure commercial precursor (*R*)-1-phenyl-2-propyn-1-ol (**22**) in three steps (Scheme 7). Upon reaction of norbornene **1** and the chiral propargylic alcohol (*R*)-**21** the diastereomeric cycloadducts **23**/**24** obtained were oxidized to the pair of enantiomers **25**/**26**. The enantiomeric excess of **25**/**26** was determined by chiral HPLC to be 80%, which was appreciably higher than the 62% obtained by **2f** in our initial studies.

Finally, the cycloaddition chemistry was applied to homopropargylic alcohols **27a–c**. Racemic homopropargylic alcohols **27a,b** were synthesized via deprotonation of ethyl propiolate (**19**) followed by trapping with an epoxide (Scheme 8), while

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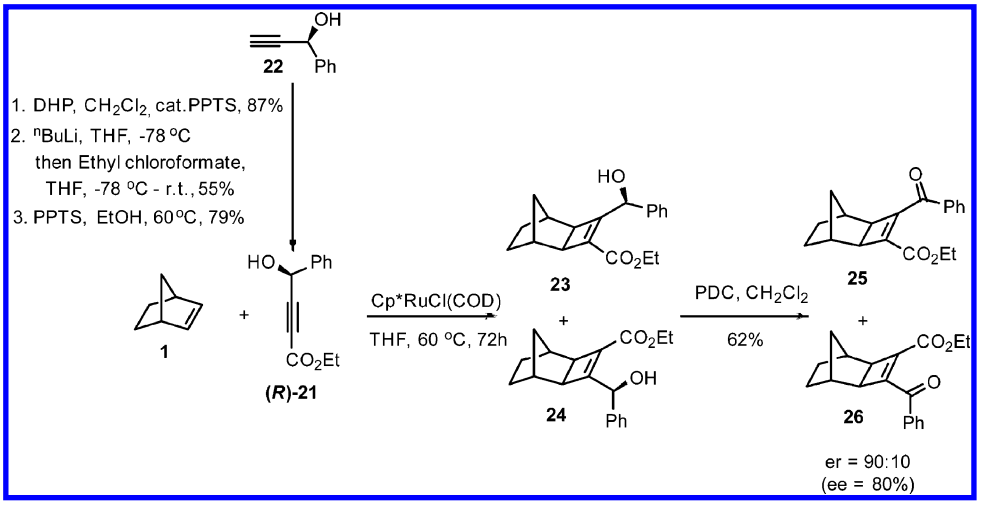
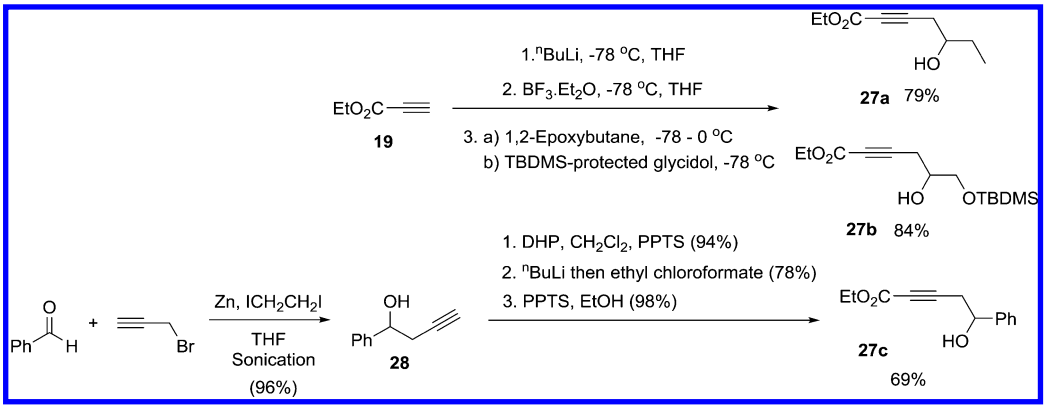
Scheme 7. Preparation and Use of a Chiral Propargylic Alcohol in Asymmetric Cycloaddition

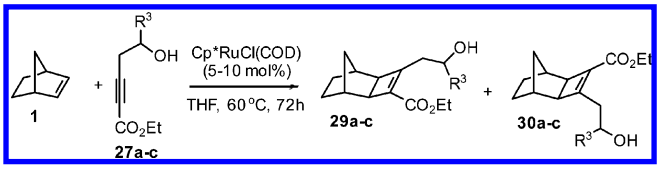


Scheme 8. Synthesis of Homopropargylic Alcohols 27a–c



alcohol **27c** was prepared from the benzylic alcohol **28** via a Barbier-type reaction. The results of cycloaddition between **1** and **27a–c** are summarized in Table 4. Excellent yields of

Table 4. Ru-Catalyzed [2 + 2] Cycloadditions between Norbornene 1 and Homopropargylic Alcohols 27a–c



entry	alcohol	R^3	yield[a] (%)	dr[b]
1	**27a**	Et	91	63:37
2	**27b**	$CH_2OTBDMS$	92	56:44
3	**27c**	Ph	89	72:28

[a]Isolated yields after column chromatography. [b]Diastereomeric ratios (dr) were determined by GC and/or ^1H NMR (400 MHz).

cycloadducts **29**/**30** were obtained for all three trials involving the homopropargylic alcohols. To the best of our knowledge, these are the first examples of Ru-catalyzed [2 + 2] cycloadditions between a bicyclic alkene and a homopropargylic alcohol. In comparison to the propargylic alcohols (Tables 2 and 3), the effects of the R^3 substituent on diastereoselectivity were not as pronounced. As the propargylic data were more desirable, we chose not to pursue homopropargylic species further for the current study. It is possible that this reduced diastereoselectivity is a result of the increased distance between the stereocenter and the reaction site, which exerts less steric control over the preferential formation of one diastereomer. However, it is also conceivable that a geometric requirement must be met in order to achieve high diastereoselectivity, which is not possible with the homopropargylic alcohols.

As mentioned, the reaction mechanism is predicted to involve hydrogen bonding of the alcohol hydrogen with the chloride ligand, which stabilizes the transition state. On the basis of calculations performed on the interactions of norbornadiene with a model propargylic alcohol (R^1 = COOEt, R^2 = H), we have learned that, over the course of the reaction, the most stable conformation between bicycloalkene and alkyne involves a geometrically restricted six-membered ring consisting of the atoms Cl–Ru–C^a–C^b–O–H in structures **31a–d** (Figure 2).[39] As the size of the R^2 substituent is increased, a greater distortion in the cyclic arrangement is expected, since C^b bearing the R^2 group will rotate to relieve steric strain. As a result, we suggest that the cycloaddition of norbornene with propargylic alcohols is highly dependent on the size of the R^2 substituent, which causes the reaction to become biased toward the formation of one diastereomer over the other. This is consistent with our experimental findings of R^2 substituents providing higher diastereoselectivity than R^1 substituents, which do not participate in the six-membered interaction. With homopropargylic R^3 substituents, a similar argument can be made in that this

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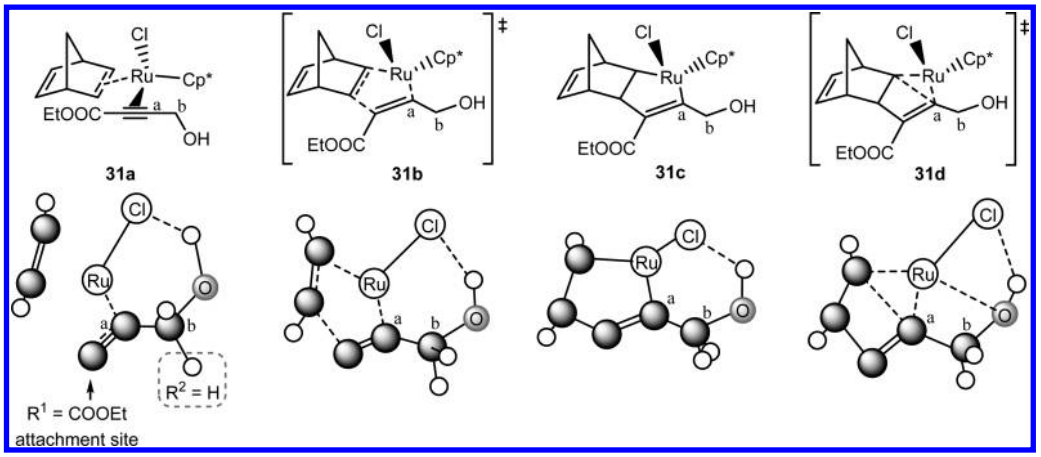
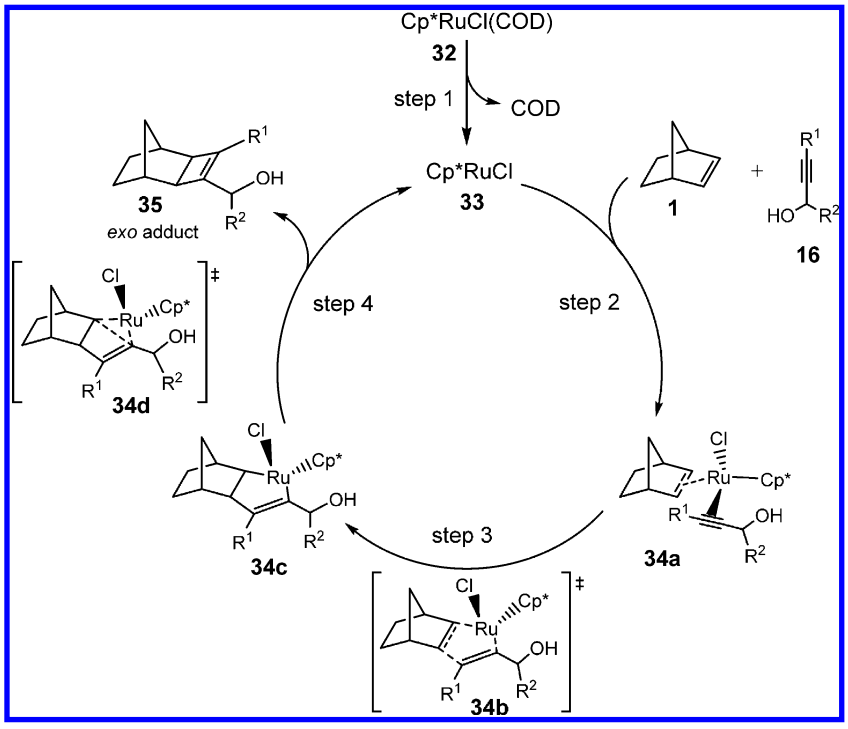


Figure 2. Predicted intramolecular hydrogen-bonding structures in the ruthenium-catalyzed [2 + 2] cycloaddition of norbornadiene with homopropargylic alcohol (R^1 = COOEt, R^2 = H): **31a**, prereaction π complex; **31b**, oxidative coupling transition state; **31c**, ruthenacyclopentene; **31d**, reductive elimination transition state (see Scheme 9 for details using the analogous structures **34a–d**).

Scheme 9. Proposed Catalytic Cycle for Cp*RuCl(COD)-Catalyzed [2 + 2] Cycloaddition between Norbornene 1 and Propargylic Alcohols 16



stereoselective arrangement is not permitted with the added carbon atom.

Scheme 9 depicts our proposed mechanism for the Ru-catalyzed [2 + 2] cycloaddition between norbornene and propargylic alcohols. Initially, dissociation of a COD ligand from Cp*RuCl(COD) **32** yields the active catalytic species, Cp*RuCl **33** (step 1). The unsaturated ruthenium coordinates with the alkene of **1** and alkyne of **16** (step 2) to form π complex **34a**. Oxidative coupling via the rate-determining transition state **34b** affords ruthenacyclopentene **34c** (step 3). Successive reductive elimination through **34d** provides representative exo cycloadduct **35** and regenerates the active catalyst **33** (step 4). The exo product is favored due to the higher π-electron density and steric accessibility of the exo face of **1** over its endo face, which in effect promotes the coordination of ruthenium preferentially to this face.[33]

CONCLUSION

In summary, we have investigated the scope of diastereoselective ruthenium-catalyzed [2 + 2] cycloadditions between norbornene and propargylic alcohols or their derivatives. We have reassessed and confirmed the previously undetermined structures of the major diastereomers from our preliminary work by X-ray diffraction analysis and have performed cycloadditions between norbornene and propargylic, acetylenic, or homopropargylic alcohols to investigate the effects of substituents on diastereoselectivity. High stereoselectivity was observed in all cases, providing exo cycloadducts with diastereoselectivity as high as 92:8 for the bulky *t*-Bu acetylenic alcohol. Furthermore, using a chiral propargylic alcohol, enantioselectivity up to 80% ee of the cycloadducts was attained upon oxidation of the alcohol. The first examples of [2 + 2] cycloaddition between norbornene and

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homopropargylic alcohols were also demonstrated, suggesting that the sterics of substituent groups play an important role in the diastereoselectivity of cycloaddition.

EXPERIMENTAL SECTION

General Information. All glassware was flame- or oven-dried, and reactions were carried out under an atmosphere of dry nitrogen at ambient temperature. Standard column chromatography was performed on 230−400 mesh silica gel using flash column chromatography techniques.[40] Analytical thin-layer chromatography (TLC) was performed on precoated silica gel 60 F_{254} plates. Chemical shifts for ^{1}H and ^{13}C NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform: δ 7.26 ppm for ^{1}H; δ 77.0 ppm for ^{13}C). GC analyses were performed using an HP-1 (methyl siloxane) column, with initial temperature 100 °C, helium flow rate 1.6 mL/min, pressure 9.52 psi, ramping 5 °C/min, final temperature 280 °C, hydrogen flow rate 40 mL/min, and air flow rate 450 mL/min. Enantiomeric ratios were determined by HPLC using the following conditions: Chiralcel OD-H column, 50/50 hexanes/2-propanol, 0.50 mL/min, 220 nm. Melting points were measured using a Mel-Temp apparatus and are uncorrected. Optical rotations were measured using an automatic polarimeter.

Reagents. Commercial reagents were used without purification. Solvents were purified by distillation under dry nitrogen from CaH_2 (dichloromethane and DMF), from molecular sieves (acetone), and from potassium/benzophenone (THF). Norbornene **1** and alkynes **17**, **18a−c**, and **19** were purchased from Aldrich. Cp*RuCl(COD) was prepared according to literature methods.[41] For complete experimental procedures and full characterization data of alkynes, see the Supporting Information sections of our previous reports.[42,43]

General Procedure for Ru-Catalyzed [2 + 2] Cycloaddition. A mixture of norbornene **1** (2.5−5 equiv), alkyne (1 equiv), and THF in an oven-dried vial was placed via a cannula in an oven-dried screw-cap vial containing Cp*RuCl(COD) (weighed in a drybox, 5−10 mol %) under nitrogen. The reaction mixture was stirred in the absence of light at 60 °C for 43−150 h. The crude product was purified by column chromatography (ethyl acetate/hexanes mixture) to provide the cycloadduct.

Cycloadducts (*S*)-4a and (*S*)-5a (Table 1, Entry 1). Following the above general procedure with norbornene **1** (42.4 mg, 0.450 mmol), acetylene **2a** (32.1 mg, 0.150 mmol), THF (0.1 mL) and Cp*Ru(COD)Cl (4.8 mg, 0.016 mmol), the reaction mixture was stirred for 48 h. The crude product was purified by column chromatography (EtOAc/hexanes 1/19) to give an inseparable mixture of cycloadducts **4a** and **5a** (16.3 mg, 0.0523 mmol, 35%, dr = 40:60 measured by ^{1}H NMR and GC) as a colorless oil: R_f = 0.36 (EtOAc/hexanes 1/9); GC (HP-1 column) retention time for major isomer 22.04 min, retention time for minor isomer 22.72 min; IR (CH_2Cl_2) 3058, 2958, 2873, 1747, 1712, 1655, 1260, 1036 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.73 (q, 0.6H, J = 6.8 Hz), 5.67 (q, 0.4H, J = 6.8 Hz), 4.12−4.21 (m, 4H), 2.48−2.56 (m, 2H), 2.17 (br s, 1H), 2.15 (br s, 0.4H), 2.01 (br s, 0.6H), 1.52−1.56 (m, 2H), 1.42 (d, 1.2H, J = 6.9 Hz), 1.40 (d, 1.8H, J = 6.8 Hz), 1.25−1.32 (m, 7H), 1.02−1.07 (m, 2.4H), 0.98 (dm, 0.6H, J = 10.5 Hz); ^{13}C NMR (APT, $CDCl_3$, 100 MHz) major diastereomer δ 162.1, 158.49, 154.38, 130.8, 70.3, 63.93, 60.0, 46.2, 46.0, 34.2, 33.7, 30.46, 28.1, 27.7, 18.8, 14.2, minor diastereomer δ 162.0, 158.54, 154.41, 130.5, 71.4, 63.97, 60.0, 46.9, 45.7, 34.1, 34.0, 30.49, 27.9, 27.7, 19.0, 14.2; HRMS (EI) calcd for $C_{17}H_{24}O_5$ [M]$^+$ 308.1624, found 308.1630.

Cycloadducts (*S*)-4b and (*S*)-5b (Table 1, Entry 2). Following the above general procedure with norbornene **1** (76.7 mg, 0.81 mmol), acetylene **2b** (50 mg, 0.27 mmol), THF (0.2 mL), and Cp*Ru(COD)Cl (4.9 mg, 0.013 mmol), the reaction mixture was stirred for 62 h. The crude product was purified by column chromatography (EtOAc/hexanes 1/19) to give an inseparable mixture of cycloadducts **4b** and **5b** (24.8 mg, 0.0891 mmol, 33%, dr =40:60 measured by ^{1}H NMR and GC) as a colorless oil: R_f = 0.65 (EtOAc/hexanes 1/4); GC (HP-1 column) retention time for major isomer = 19.23 min, retention time for minor isomer 19.65 min; IR (CH_2Cl_2) 2957, 2872, 1744, 1717, 1653, 1369, 1237 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.84 (q, 0.6H, J = 6.7 Hz), 5.74 (q, 0.4H, J = 6.7 Hz), 4.13−4.19 (m, 2H), 2.53 (m, 1.6H), 2.42 (m, 0.4H), 2.18 (br s, 1H), 2.13 (br s, 0.4H), 2.07 (s, 1.2H), 2.05 (s, 1.8H), 1.98 (br s, 0.6H), 1.54−1.58 (m, 2H), 1.39 (d, 1.2H, J = 6.8 Hz), 1.36 (d, 1.8H, J = 6.8 Hz), 1.34 (m, 1H, J = 12.6 Hz), 1.28 (t, 3H, J = 7.1 Hz), 1.06−0.99 m, 3H, J = 7.4 Hz); ^{13}C NMR (APT, $CDCl_3$, 100 MHz) major diastereomer δ 170.1, 162.2, 158.9, 130.6, 67.1, 60.0, 46.3, 46.0, 34.3, 33.8, 30.4, 28.1, 28.0, 21.0, 18.8, 14.3, minor diastereomer δ 170.1, 162.2, 159.3, 130.4, 68.0, 60.0, 47.1, 45.6, 34.09, 34.04, 30.6, 28.2, 27.8, 21.0, 19.0, 14.3; HRMS (EI) calcd for $C_{16}H_{22}O_4$ [M]$^+$ 278.1518, found 278.1527.

Cycloadducts (*S*)-4c and (*S*)-5c (Table 1, Entry 3). Following the above general procedure with norbornene **1** (36.8 mg, 0.392 mmol), acetylene **2c** (28.4 mg, 0.123 mmol), THF (0.1 mL), and Cp*Ru(COD)Cl (3.8 mg, 0.012 mmol), the reaction mixture was stirred for 72 h. The crude product was purified by column chromatography (EtOAc/hexanes 1/17) to give an inseparable mixture of cycloadducts **4c** and **5c** (18 mg, 0.055 mmol, 45%, dr = 42:58 measured by ^{1}H NMR and GC) as a colorless oil: R_f = 0.29 (EtOAc/hexanes 3/7); GC (HP-1 column) retention time for major isomer 24.94 min, retention time for minor isomer 25.17 min; IR (CH_2Cl_2) 2956, 2872, 2814, 1717, 1650, 1455 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.87 (q, 1H, J = 6.7 Hz), 4.72 (br s, 1H), 4.70 (d, 1H, J = 2.2 Hz), 4.13−4.19 (m, 2H), 3.74−3.78 (m, 1H), 3.60−3.66 (m, 1H), 3.54−3.57 (m, 2H), 3.39 (s, 1.7H), 3.38 (s, 1.3H), 2.54 (m, 2H), 2.18 (br s, 1H), 2.15 (br s, 0.4H), 2.11 (br s, 0.6H), 1.55−1.57 (m, 2H), 1.25−1.34 (m, 8H), 1.08 (dm, 1.2H, J = 6.9 Hz), 1.02 (dm, 0.8H, J = 10.5 Hz); ^{13}C NMR (APT, $CDCl_3$, 100 MHz) major diastereomer δ 162.4, 161.7, 130.6, 93.7, 71.7, 68.2, 66.8, 59.8, 58.9, 45.96, 45.86, 34.2, 33.6, 30.5, 28.1, 27.9, 19.4, 14.2, minor diastereomer δ 162.4, 161.6, 131.2, 93.8, 71.7, 68.8, 66.9, 59.8, 58.9, 46.9, 45.6, 34.3, 34.0, 30.4, 28.2, 27.8, 19.7, 14.2; HRMS (EI) calcd for $C_{18}H_{28}O_5$ [M]$^+$ 324.1937, found 324.1943.

Cycloadducts (*S*)-4d and (*S*)-5d (Table 1, Entry 4). Following the above general procedure with norbornene **1** (18.1 mg, 0.192 mmol), alkyne **2d** (10.5 mg, 0.045 mmol), THF (0.20 mL) and Cp*RuCl(COD) (1.7 mg, 0.004 mmol), the reaction mixture was stirred for 150 h. The crude product was purified by column chromatography (EtOAc/hexanes 0/1, 1/19, 1/9) to give an inseparable mixture of cycloadducts **4d** and **5d** (7.0 mg, 0.021 mmol, 47%, dr = 29:71 measured by GC) as a colorless oil: R_f = 0.40 (EtOAc/hexanes 1/9); $[\alpha]_D^{25}$ = −14.1° (c = 0.085, $CHCl_3$); GC (HP-1 column) retention time for major isomer 28.008 min and retention time for minor isomer 28.241 min; IR (neat) 3031, 2956, 2871, 1747, 1713, 1652, 1558, 1496, 1455, 1368, 1328, 1228, 1190, 1116, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34 (s, 1.16H), 7.33 (s, 2.84H), 7.28 (m, 1H), 4.68 (q, 0.29H, J = 6.5 Hz), 4.66 (q, 0.71H, J = 6.6 Hz), 4.58 (d, 0.71H, J = 11.8 Hz), 4.55 (d, 0.29H, J = 11.8 Hz), 4.45 (d, 0.71H, J = 11.8 Hz), 4.41 (d, 0.29H, J = 11.8 Hz), 4.164 (q, 0.58H, J = 7.1 Hz), 4.161 (q, 1.42H, J = 7.1 Hz), 2.60 (s, 0.58H), 2.58 (d, 0.71H, J = 3.4 Hz), 2.56 (d, 0.71H, J = 3.4 Hz), 2.21 (m, 2H), 1.58 (m, 2H), 1.48 (dm, 1H, J = 10.4 Hz), 1.33 (d, 0.87H, J = 6.5 Hz), 1.31 (d, 2.13H, J = 6.6 Hz), 1.26 (t, 3H, J = 7.1 Hz), 1.11 (m, 2.71H), 1.05 (dm, 0.29H, J = 10.4 Hz); ^{13}C NMR (APT, $CDCl_3$, 150 MHz) major isomer δ 162.64, 162.45, 138.6, 131.6, 128.3, 127.7, 127.5, 71.4, 70.7, 59.8, 46.0, 45.9, 34.5, 33.6, 30.9, 28.31, 28.0, 19.5, 14.3, visible peaks for minor isomer δ 162.60, 162.37, 138.5, 132.4, 128.6, 127.5, 71.1, 71.0, 46.9, 45.8, 34.6, 34.2, 30.6, 28.28, 27.9, 19.7; HRMS calcd for $C_{21}H_{26}O_3$ [M]$^+$ 326.1882, found 326.1870.

Cycloadducts (*S*)-4e and (*S*)-5e (Table 1, Entry 5). Following the above general procedure with norbornene **1** (55.9 mg, 0.594 mmol), alkyne **2e** (25.1 mg, 0.098 mmol), THF (0.20 mL) and Cp*RuCl(COD) (3.7 mg, 0.010 mmol), the reaction mixture was stirred for 43 h. The crude product was purified by column chromatography (EtOAc/hexanes 0/1, 3/97, 1/19) to give an inseparable mixture of cycloadducts **4e** and **5e** (22.3 mg, 0.064 mmol, 65%, dr = 32:68 measured by GC) as a colorless oil: R_f = 0.45 (EtOAc/hexanes 1/19); $[\alpha]_D^{22}$ = +17.1° (c = 0.58, $CHCl_3$); GC (HP-1 column): retention time for major isomer 23.320 min and retention time for minor isomer 22.790 min; IR (neat) 2964, 2933, 2866, 1722, 1655, 1470, 1368, 1336, 1264, 1229, 1192, 1130, 1084, 1048 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.97 (q, 0.73H, J = 6.4 Hz), 4.92 (q, 0.27H, J = 6.6 Hz), 4.16 (qd, 2H, J = 7.1, 2.3 Hz), 2.54 (d, 0.27H, J = 3.2 Hz), 2.51 (dm, 1.73H, J = 3.7 Hz), 2.21 (s, 1.27H),

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2.17 (s, 0.73H), 1.53−1.60 (m, 2H), 1.39 (dm, 1H, J = 10.2 Hz), 1.28 (t, 3H, J = 7.1 Hz), 1.27 (d, 0.81H, J = 6.6 Hz), 1.24 (d, 2.19H, J = 6.4 Hz), 1.07 (m, 2H), 0.99 (dm, 1H, J = 10.2 Hz), 0.88 (s, 9H), 0.07 (s, 2.19H), 0.04 (s, 3H), 0.03 (s, 0.81H); ^{13}C NMR (APT, $CDCl_3$, 100 MHz) major isomer δ 164.3, 162.7, 127.8, 64.5, 59.7, 45.9, 45.7, 34.6, 34.0, 30.6, 28.2, 28.1, 25.8, 22.5, 18.1, 14.3, −4.85, −5.00, visible peaks for minor isomer: δ 165.2, 65.3, 46.8, 45.3, 34.4, 34.2, 30.5, 28.3, 27.9, 22.9, −4.91, −4.96. Anal. Calcd for $C_{20}H_{34}O_3Si$: C, 68.52; H, 9.78. Found C, 68.17; H, 9.97.

Cycloadducts (*S*)-4f and (*S*)-5f (Table 1, Entry 6). Following the above general procedure with norbornene **1** (159 mg, 1.69 mmol), acetylene **2f** (80 mg, 0.56 mmol), THF (0.3 mL), and Cp*Ru(COD)Cl (13.3 mg, 0.035 mmol), the reaction mixture was stirred at 60 °C for 72 h to afford an inseparable mixture of cycloadducts **4f** and **5f**: 93.1 mg, 0.40 mmol, 71% yellow oil; dr = 81:19 (measured by ^{1}H NMR and GC). For characterization data, see our previous report.[19]

Cycloadducts 7 and 8 (Scheme 2). Following the above general procedure with alkene **6** (90.1 mg, 0.349 mmol), alkyne **2f** (35.1 mg, 0.246 mmol), THF (0.6 mL), and Cp*Ru(COD)Cl (5.6 mg, 0.015 mmol), the reaction mixture was stirred for 1 h. The crude product was purified by column chromatography (gradient EtOAc/hexanes 1/19 to 2/3) to provide **7** and **8** as an inseparable mixture (73.2 mg, 0.183 mmol, 74%, dr = 91:9 measured by ^{1}H NMR). **7** (major diastereomer): R_f = 0.19 (EtOAc/hexanes 3/7); IR (CH_2Cl_2) 3415, 2983, 2907, 1762, 1681, 1673, 1202 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.78 (m, 2H), 4.79 (br s, 1H), 4.59 (br q, 1H, J = 6.7 Hz), 4.23 (q, 2H, J = 7.1 Hz), 3.18 (br s, 1H), 3.05 (br s, 1H), 2.76 (br d, 1H, J = 3.1 Hz), 2.70 (br d, 1H, J = 3.2 Hz), 2.31 (s, 3H), 2.30 (s, 3H), 1.77 (br s, 2H), 1.35 (d, 3H, J = 6.6 Hz), 1.32 (t, 3H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.2, 169.1,167.9, 163.7, 142.3, 140.3, 139.8, 129.8, 120.5, 120.3, 65.7, 61.0, 44.2, 42.9, 40.6, 38.4, 37.9, 21.5, 20.84, 20.74, 14.1; HRMS (CI) calcd for $C_{22}H_{24}O_7$ $[M + H]^+$ 401.1600, found 401.1608.

Cycloadducts 9 and 10 (Scheme 2). To a solution of **7** and **8** (42.1 mg, 0.105 mmol) in pyridine (0.3 mL) was added 4-nitrobenzoyl chloride (38.4 mg, 0.207 mmol). The reaction mixture was stirred at room temperature for 1.5 h, diluted with ethyl acetate, and washed three times with saturated copper sulfate aqueous solution and once with water. The organic layer was dried over Na_2SO_4, concentrated, and purified by column chromatography (gradient EtOAc/hexanes 1/10 to 2/3) to give a mixture of **9** and **10** (56.3 mg, 0.102 mmol, 96%) as a white solid. The pure major diastereomer **9** was obtained through fractional recrystallization (Et_2O/hexanes, three times): IR (CH_2Cl_2) 2979, 2954, 1763, 1725, 1529, 1269 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.26−8.32 (m, 4H), 6.81 (d, 1H, J = 8.8 Hz), 6.77 (d, 1H, J = 8.8 Hz), 6.07 (q, 1H, J = 6.8 Hz), 4.22 (q, 2H, J = 7.1 Hz), 3.27 (s, 1H), 3.16 (s, 1H), 2.85 (br d, 1H, J = 3.4 Hz), 2.82 (br d, 1H, J = 3.4 Hz), 2.32 (s, 3H), 2.18 (s, 3H), 1.84 (m, 2H), 1.63 (d, 3H, J = 6.8 Hz), 1.32 (t, 3H, J = 7.1 Hz); ^{13}C NMR (APT, $CDCl_3$, 75 MHz) δ 169.2, 168.7, 163.8, 161.7, 158.5, 150.6, 142.6, 142.3, 140.1, 139.8, 135.6, 131.5, 130.9, 123.5, 120.7, 120.2, 69.5, 60.4, 44.3, 43.3, 40.6, 38.6, 38.4, 20.9, 20.7, 19.1, 14.3; HRMS (CI) calcd for $C_{29}H_{27}NO_{10}$ $[M + H]^+$ 549.1635, found 549.1641.

Oxidized Cycloadducts 11f and 12f (Scheme 4). For characterization, see our previous report.[19]

Cycloadducts 19c and 20c (Table 2, Entry 2). Following the above general procedure with norbornene **1** (77.1 mg, 0.819 mmol), propargylic alcohol **16c** (45.8 mg, 0.269 mmol), THF (0.4 mL), and Cp*RuCl(COD) (11.0 mg, 0.0289 mmol), the reaction mixture was stirred for 72 h. The crude product was purified by column chromatography (EtOAc/hexanes 1/9) to provide an inseparable mixture of cycloadducts **19c** and **20c** (52.9 mg, 0.200 mmol, 74%, dr = 78:22 measured by ^{1}H NMR) as a colorless oil: R_f = 0.38 (EtOAc/Hexanes 1/9); IR (neat, NaCl) 3446, 2960, 2875, 1714, 1370, 1257 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.24 (br s, 1H), 4.44 (q, 1H, J = 6.7 Hz), 2.47 (br s, 1H), 2.37−2.38 (m, 0.78H), 2.30−2.31 (m, 0.22H), 2.12 (br s, 1H), 1.99 (br s, 1H), 1.53−1.56 (m, 2H), 1.50 (s, 1.98H), 1.47 (s, 7.02H), 1.28 (d, 3H, J = 6.9 Hz), 0.98−1.11 (m, 4H); ^{13}C NMR (APT, $CDCl_3$, 75 MHz) major isomer δ 166.5, 163.7, 130.6, 81.4, 65.4, 46.6, 45.8, 33.9, 33.4, 30.43, 28.1, 27.9, 21.3; visible peaks for minor isomer δ 81.8, 67.1, 47.2, 46.0, 34.1, 33.8, 30.37, 28.0, 21.7; HRCI calcd for $C_{16}H_{24}O_3$ $[M + H]^+$ 265.1804, found 265.1811.

Cycloadducts 19g and 20g (Table 2, Entry 3). Following the above general procedure with norbornene **1** (242.2 mg, 2.572 mmol), propargylic alcohol **16g** (132.1 mg, 0.9036 mmol), THF (1.8 mL), and Cp*RuCl(COD) (20.4 mg, 0.0537 mmol), the reaction mixture was stirred for 72 h. The crude product was purified by column chromatography (EtOAc/hexanes 2/8) to provide a separable mixture of cycloadducts **19g** and **20g** (123.3 mg, 0.5130 mmol, 57%, dr = 64:36 measured by GC) as a yellow oil: R_f for major isomer 0.43 (EtOAc/hexanes 2/8), R_f for minor isomer 0.53 (EtOAc/hexanes 2/8); GC (HP-1 column) retention time for major isomer 21.65 min, retention time for minor isomer 21.28 min; IR (CH_2Cl_2, NaCl) major isomer 3387, 2950, 2869, 1492, 1447, 1368, 1297, 1061 cm^{-1}, minor isomer 3382, 2949, 2920, 2867, 1492, 1447, 1296, 1061 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) major isomer 7.30−7.38 (m, 4H), 7.21−7.25 (m, 1H), 4.86 (q, 1H, J = 6.6 Hz), 2.68−2.69 (m, 1H), 2.62−2.63 (m, 1H), 2.19 (br s, 1H), 2.16 (br s, 1H), 1.67 (br s, 1H), 1.58−1.65 (m, 2H), 1.44−1.46 (m, 1H), 1.40 (d, 3H, J = 6.6 Hz), 1.12−1.19 (m, 2H), 1.00−1.03 (m, 1H), minor isomer δ 7.39−7.43 (m, 2H), 7.32−7.35 (m, 2H), 7.16−7.25 (m, 1H), 4.83 (q, 1H, J = 6.5 Hz), 2.68−2.69 (m, 1H), 2.54−2.55 (m, 1H), 2.20 (br s, 1H), 2.18 (br s, 1H), 1.58−1.63 (m, 3H), 1.52−1.55 (m, 1H), 1.39 (d, 3H, J = 6.5 Hz), 1.12−1.19 (m, 2H), 1.03−1.05 (m, 1H); ^{13}C NMR (APT, $CDCl_3$, 75 MHz) major isomer δ 144.4, 138.8, 134.4, 128.4, 127.2, 126.8, 64.8, 45.9, 45.5, 34.9, 34.6, 30.6, 28.6, 28.3, 21.7, minor isomer δ 144.3, 139.0, 134.4, 128.4, 127.2, 126.8, 65.1, 45.8, 45.5, 35.2, 34.6, 30.6, 28.7, 28.3, 21.4; HRCI calcd for $C_{17}H_{20}O$ $[M + H]^+$ 241.1592, found for major isomer 241.1597, found for minor isomer 241.1588.

Cycloadducts 19e and 20e (Table 2, Entry 4). Following the above general procedure with norbornene **1** (119.5 mg, 1.269 mmol), propargylic alcohol **16e** (50.1 mg, 0.397 mmol), THF (0.8 mL), and Cp*RuCl(COD) (11.6 mg, 0.0305 mmol), the reaction mixture was stirred for 72 h. The crude product was purified by column chromatography (EtOAc/hexanes 1/9) to provide an inseparable mixture of cycloadducts **19e** and **20e** (77.8 mg, 0.353 mmol, 88%, dr = 82:12 measured by GC) as a yellow oil: R_f 0.35 (EtOAc/hexanes 1/9); GC (HP-1 column) retention time for major isomer 14.78 min, retention time for minor isomer 14.47 min; IR (neat, NaCl) 3328, 2950, 2868, 1449, 1366, 1296, 1316, 1082 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.41 (q, 1H, J = 6.5 Hz), 2.39 (br s, 1H), 2.23 (br s, 1H), 1.98−2.06 (m, 3H), 1.95 (br s, 1H), 1.41−1.57 (m, 4H), 1.28−1.40 (m, 4H), 1.25 (d, 0.54H, J = 6.5 Hz), 1.24 (d, 2.46H, J = 6.6 Hz), 0.92−1.01 (m, 3H), 0.88 (t, 3H, J = 7.1 Hz); ^{13}C NMR (APT, $CDCl_3$, 75 MHz) major isomer δ 143.1, 142.5, 64.7, 47.3, 45.4, 34.8, 34.1, 30.4, 29.9, 28.4, 27.2, 22.9, 22.1, 13.9, visible peaks for minor isomer δ 64.2, 47.1, 45.3, 34.7, 27.3, 21.9; HRCI calcd for $C_{15}H_{24}O$ $[M + H]^+$ 221.1905, found 221.1911.

Cycloadducts 19f and 20f (Table 2, Entry 5). Following the above general procedure with norbornene **1** (36.5 mg, 0.388 mmol), propargylic alcohol **16f** (18.0 mg, 0.117 mmol), THF (0.2 mL), and Cp*RuCl(COD) (6.0 mg, 0.016 mmol), the reaction mixture was stirred for 72 h. The crude product was purified by column chromatography (EtOAc/hexanes 1/9) to provide an inseparable mixture of cycloadducts **19f** and **20f** (13.1 mg, 0.0527 mmol, 44%, dr = 77:23 measured by ^{1}H NMR) as a pale yellow oil: R_f 0.45 (EtOAc/hexanes 1/9); IR (neat, NaCl) 3303, 2951, 2926, 2869, 1453 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.43 (q, 1H, J = 6.6 Hz), 2.40 (br s, 0.77H), 2.34 (br s, 0.23H), 2.24−2.25 (m, 1H), 1.99−2.06 (m, 3H), 1.96 (br s, 1H), 1.60 (br s, 1H), 1.51−1.54 (m, 2H), 1.35−1.43 (m, 2H), 1.25−1.30 (m, 11H), 0.94−1.03 (m, 2H), 0.88 (t, 3H, J = 7.1 Hz); ^{13}C NMR (APT, $CDCl_3$, 75 MHz) major isomer δ 143.2, 142.5, 64.3, 47.4, 45.4, 34.9, 34.2, 31.7, 30.5, 29.5, 28.4, 27.7, 27.5, 22.6, 22.1, 14.1, visible peaks for minor isomer δ 143.1, 64.7, 47.1, 45.3, 34.8, 22.0; HRCI calcd for $C_{17}H_{28}O$ $[M + H]^+$ 249.2218, found 249.2212.

Cycloadducts 19a and 20a (Table 2, Entry 6). Following the above general procedure with norbornene **1** (228.9 mg, 2.431 mmol), propargylic alcohol **16a** (80.7 mg, 0.806 mmol), THF (1.0 mL), and Cp*RuCl(COD) (32.6 mg, 0.0858 mmol), the reaction mixture was stirred for 72 h. The crude product was purified by column chromatography (EtOAc/hexanes 4/6) to provide an inseparable mixture of cycloadducts **19a** and **20a** (95.4 mg, 0.491 mmol, 61%, dr = 55:45 determined by GC from the acetylated cycloadducts) as a yellow

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oil: R_f 0.23 (EtOAc/hexanes 4/6); IR (neat, NaCl) 3301, 2948, 2869, 1451, 1368, 1318, 1297, 1265 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 4.30−4.36 (m, 1H), 4.085−4.092 (m, 2H), 2.30−2.32 (m, 1H), 2.24 (br s, 1H), 2.01 (br s, 0.5H), 1.94 (br s, 1.5H), 1.50−1.55 (m, 2.5H), 1.43−1.46 (m, 0.5H), 1.28 (d, 1.5H, J = 6.4 Hz), 1.26 (d, 1.5H, J = 6.4 Hz), 0.96−1.03 (m, 3H); ^{13}C NMR (APT, $CDCl_3$, 75 MHz) major isomer δ 144.1, 139.1, 64.4, 59.1, 46.1, 45.7, 33.8, 30.4, 28.2, 22.0, visible peaks for minor isomer δ 143.9, 139.6, 66.2, 59.2, 46.7, 45.9, 34.6, 33.6, 30.3, 28.3, 22.5; HRCI calcd for $C_{12}H_{18}O_2$ $[M + H]^+$ 195.1385, found 195.1380.

Cycloadducts 19b and 20b (Table 2, Entry 7). Following the above general procedure with norbornene **1** (318.3 mg, 3.380 mmol), propargylic alcohol **16b** (141.9 mg, 1.107 mmol), THF (1.2 mL), and Cp*RuCl(COD) (32.1 mg, 0.0845 mmol), the reaction mixture was stirred for 72 h. The crude product was purified by column chromatography (EtOAc/hexanes 4/6) to provide an inseparable mixture of cycloadducts **27i** and **28i** (137.7 mg, 0.6194 mmol, 56%, dr = 50:50 determined by GC from the acetylated cycloadducts) as a yellow oil: R_f 0.38 (EtOAc/hexanes 4/6); IR (neat, NaCl) 3208, 2958, 2869, 1449, 1374, 1359, 1316, 1004 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 4.67 (br s, 2H), 4.28−4.35 (m, 1H), 2.27 (d, 1H, J = 2.5 Hz), 2.18−2.22 (m, 1H), 2.00 (br s, 0.5H), 1.97 (br s, 1H), 1.92 (br s, 0.5H), 1.48−1.59 (m, 3H), 1.32 (s, 1.5H), 1.30 (s, 1.5H), 1.292 (s, 1.5H), 1.290 (s, 1.5H), 1.27 (d, 1.5H, J = 6.7 Hz), 1.24 (d, 1.5H, J = 6.7 Hz), 0.93−1.03 (m, 3H); ^{13}C NMR (APT, $CDCl_3$, 75 MHz) δ 146.3, 145.8, 141.9, 141.7, 70.5, 66.1, 64.3, 46.0, 45.9, 45.6, 44.9, 34.9, 34.5, 34.4, 33.9, 30.23, 30.18, 30.1, 29.6, 29.2, 28.9, 28.4, 28.3, 22.6, 22.2; HRCI calcd for $C_{14}H_{22}O_2$ $[M + H]^+$ 223.1698, found 223.1705.

Cycloadducts 19h and 20h (Table 3, Entry 2). Following the above general procedure with norbornene **1** (158.0 mg, 1.678 mmol), propargylic alcohol **16h** (111.9 mg, 0.548 mmol), THF (0.80 mL), and Cp*RuCl(COD) (17.3 mg, 0.0455 mmol), the reaction mixture was stirred for 72 h. The crude product was purified by column chromatography (EtOAc/hexanes 1/9) to provide an inseparable mixture of cycloadducts **19h** and **20h** (121.3 mg, 0.4065 mmol, 74%, dr = 90:10 measured by HPLC from the oxidized cycloadducts) as a yellow oil: R_f = 0.41 (EtOAc/hexanes 1/9); IR (neat, NaCl) 3382, 2956, 2872, 1712, 1679, 1451, 1369, 1285, 1215, 1057, 1026 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, no visible peaks for minor isomer) δ 7.26−7.43 (m, 5H), 6.02 (br s, 1H), 5.32 (s, 1H), 4.25 (q, 2H, J = 7.1 Hz), 2.51 (d, 1H, 2.3 Hz), 2.20 (d, 1H, J = 3.3 Hz), 2.18 (br s, 1H), 2.05 (br s, 1H), 1.47−1.61 (m, 2H), 1.40−1.44 (m, 1H), 1.33 (t, 3H, J = 7.1 Hz), 0.96−1.08 (m, 3H); ^{13}C NMR (APT, $CDCl_3$, 75 MHz, no visible peaks for minor isomer) δ 165.7, 164.3, 141.2, 129.3, 128.5, 127.7, 126.4, 72.6, 60.9, 47.2, 45.8, 33.9, 33.5, 30.5, 27.9, 27.8, 14.2; HRCI calcd for $C_{19}H_{22}O_3$ $[M + H]^+$ 299.1647, found 299.1640.

Cycloadducts 19i and 20i (Table 3, Entry 3). Following the above general procedure with norbornene **1** (62.2 mg, 0.661 mmol), propargylic alcohol **16i** (41.6 mg, 0.226 mmol), THF (0.30 mL), and Cp*RuCl(COD) (7.4 mg, 0.019 mmol), the reaction mixture was stirred for 72 h. The crude product was purified by column chromatography (EtOAc/hexanes 1/9) to provide a separable mixture of cycloadducts **19i** and **20i** (50.5 mg, 0.181 mmol, 75%, dr = 92:8 measured by GC) as a yellow oil: R_f for major isomer 0.47 (EtOAc/hexanes 1/9), R_f for minor isomer 0.32 (EtOAc/hexanes 1/9); GC (HP-1 column): retention time for major isomer 20.71 min, retention time for minor isomer 20.93 min; IR (neat, NaCl) major isomer 3412, 2954, 2871, 1682, 1631, 1367, 1284, 1217 cm^{-1}, minor isomer 3517 (m), 2954 (s), 2871 (m), 1712 (s), 1694 (s), 1642 (m), 1478 (m), 1393 (w), 1367 (m), 1264 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) major isomer δ 5.29 (d, 1H, J = 9.3 Hz), 4.20 (dq, 2H, J = 7.1, 2.3 Hz), 3.72 (d, 1H, J = 9.3 Hz), 2.60 (d, 1H, J = 2.6 Hz), 2.44, (d, 1H, J = 2.9 Hz), 2.14 (br s, 1H), 2.09 (br s, 1H), 1.57−1.60 (m, 2H), 1.36−1.39 (m, 1H), 1.30 (t, 3H, J = 7.1 Hz), 1.01−1.09 (m, 3H), 0.95 (s, 9H), minor isomer δ 4.16−4.20 (m, 3H), 3.29 (d, 1H, J = 7.4 Hz), 2.58 (d, 1H, J = 3.1 Hz), 2.51, (d, 1H, J = 3.1 Hz), 2.21 (br s, 1H), 2.18 (br s, 1H), 1.56−1.59 (m, 2H), 1.40−1.43 (m, 1H), 1.29 (t, 3H, J = 7.1 Hz), 1.05−1.10 (m, 3H), 0.96 (s, 9H); ^{13}C NMR (APT, $CDCl_3$, 75 MHz) major isomer δ 167.3, 164.3, 131.5, 78.2, 60.7, 50.8, 46.1, 37.3, 33.7, 33.6, 30.5, 28.1, 28.0, 26.0, 14.2, minor isomer δ 164.3, 163.5, 133.0, 78.0, 60.2, 49.7, 46.2, 36.3, 35.0, 33.8, 30.7, 28.14, 28.09, 26.1, 14.2; HRCI calcd for $C_{17}H_{26}O_3$ $[M + H]^+$ 279.1960, found for major isomer 279.1963, found for minor isomer 279.1958.

Cycloadducts 19j and 20j (Table 3, Entry 4). Following the above general procedure with norbornene **1** (199.0 mg, 2.11 mmol), propargylic alcohol **16j** (153.1 mg, 0.728 mmol), THF (1.0 mL), and Cp*RuCl(COD) (26.3 mg, 0.0692 mmol), the reaction mixture was stirred for 72 h. The crude product was purified by column chromatography (EtOAc/hexanes 1/9) to provide a separable mixture of cycloadducts **19j** and **20j** (218.5 mg, 0.7178 mmol, 98%, dr = 88:12 measured by ^1H NMR) as a yellow oil: R_f for major isomer 0.46 (EtOAc/hexanes 1/9), R_f for minor isomer 0.35 (EtOAc/hexanes 1/9); IR (neat, NaCl) major isomer 3416, 2929, 2870, 2854, 1714, 1682, 1634, 1451, 1369, 1299, 1285 cm^{-1}, minor isomer 3425, 2928, 2869, 2853, 1712, 1682, 1636, 1450, 1369, 1303, 1284, 1214 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) major isomer δ 5.16 (br s, 1H), 4.19 (dq, 2H, J = 7.1, 1.1 Hz), 4.03 (br s, 1H), 2.57 (d, 1H, J = 2.2 Hz), 2.39 (d, 1H, J = 3.1 Hz), 2.15 (br s, 1H), 2.04 (br s, 1H), 1.74−1.78 (m, 2H), 1.46−1.63 (m, 6H), 1.39 (br s, 1H), 1.35 (br s, 1H), 1.29 (t, 3H, J = 7.1 Hz), 1.01−1.22 (m, 7H), minor isomer δ 4.76 (br s, 1H), 4.45 (br s, 1H), 4.18 (q, 2H, J = 7.1 Hz), 2.57 (br s, 1H), 2.43 (d, 1H, J = 2.9 Hz), 2.17 (br s, 1H), 2.11 (br s, 1H), 1.51−1.78 (m, 8H), 1.37−1.50 (m, 3H), 1.29 (t, 3H, J = 7.1 Hz), 1.05−1.23 (m, 6H); ^{13}C NMR (APT, $CDCl_3$, 75 MHz) major isomer δ 167.6, 164.3, 130.5, 74.2, 60.7, 48.0, 45.8, 43.5, 33.8, 33.6, 30.5, 29.3, 28.0, 27.9, 26.8, 26.4, 26.31, 26.26 14.2, minor isomer δ 166.4, 164.0, 131.1, 75.8, 60.5, 48.0, 45.9, 43.0, 34.6, 33.8, 30.8, 30.2, 28.3, 27.9, 26.6, 26.2, 26.1, 14.2; HRCI calcd for $C_{19}H_{28}O_3$ $[M + H]^+$ 305.2117, found for major isomer 305.2114, found for minor isomer: 305.2112.

Oxidized Cycloadducts 25 and 26 (Scheme 7). Following the oxidation protocol from our previous work[19] with **23** and **24** (132.8 mg, 0.4451 mmol), the reaction mixture was stirred for 36 h. This was filtered through a plug of silica and concentrated in vacuo. The crude product was purified by column chromatography (EtOAc/hexanes 1/9) to provide the oxidized adduct mixture **25** and **26** (82.6 mg, 0.279 mmol, 62%) as a yellow oil: R_f = 0.46 (EtOAc/hexanes 1/9); $[\alpha]^{24}_D$ = +59.8° (c 0.545, $CHCl_3$, 80% ee measured by HPLC); HPLC (OJ-H column, 0.50 mL/min, 1% ^{i}PrOH/hexane, 254 nm) major enantiomer 20.44 min, minor enantiomer 25.00 min; IR (neat, NaCl) 2959, 2873, 1719, 1645, 1449, 1317, 1283, 1203, 1122 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.88−7.90 (m, 2H), 7.55−7.59 (m, 1H), 7.43−7.47 (m, 2H), 3.89−3.98 (m, 2H), 2.87 (d, 1H, J = 3.1 Hz), 2.82 (d, 1H, J = 3.0 Hz), 2.35 (s, 2H), 1.56−1.67 (m, 3H), 1.11−1.18 (m, 3H), 0.86 (t, 3H, J = 7.1 Hz); ^{13}C NMR (APT, $CDCl_3$, 75 MHz) δ 191.5, 161.4, 151.1, 137.8, 136.6, 133.3, 129.2, 128.4, 60.4, 49.5, 47.0, 34.4, 34.3, 30.8, 27.9, 13.5; Anal. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.90; H, 6.94.

Cycloadducts 29a and 30a (Table 4, Entry 1). Following the above general procedure with norbornene **1** (101.9 mg, 1.082 mmol), homopropargylic alcohol **27a** (59.6 mg, 0.350 mmol), THF (0.50 mL), and Cp*RuCl(COD) (13.2 mg, 0.0347 mmol), the reaction mixture was stirred for 72 h. The crude product was purified by column chromatography (EtOAc/hexanes 2/8) to provide an inseparable mixture of cycloadducts **29a** and **30a** (83.9 mg, 0.317 mmol, 91%, dr = 63:37 measured by ^1H NMR) as a yellow oil: R_f = 0.48 (EtOAc/hexanes 2/8); IR (neat, NaCl) 3479, 2956, 2872, 1714, 1694, 1650, 1463, 1454, 1370, 1284 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.16 (q, 2H, J = 7.1 Hz), 3.74−3.76 (m, 1H), 2.97 (br s, 0.37H), 2.76 (br s, 0.63H), 2.54−2.63 (m, 2H), 2.35−2.46 (m, 2H), 2.16 (br s, 1H), 2.03 (br s, 1H), 1.46−1.62 (m, 4H), 1.28 (t, 3H, J = 7.1 Hz), 1.01−1.08 (m, 4H), 0.95 (t, 3H, J = 7.4 Hz); ^{13}C NMR (APT, $CDCl_3$, 75 MHz) major isomer δ 163.6, 161.1, 132.1, 71.1, 59.89, 48.9, 46.4, 37.0, 33.9, 33.4, 30.6, 30.5, 28.1, 27.9, 14.3, 9.9; visible peaks for minor isomer δ 163.7, 161.2, 32.0, 71.6, 59.94, 49.7, 37.2, 34.0, 33.6; HRCI calcd for $C_{16}H_{24}O_3$ $[M + H]^+$ 265.1810, found 265.1804.

Cycloadducts 29b and 30b (Table 4, Entry 2). Following the above general procedure with norbornene **1** (48.0 mg, 0.510 mmol), homopropargylic alcohol **27b** (53.8 mg, 0.188 mmol), THF (0.30 mL), and Cp*RuCl(COD) (9.6 mg, 0.025 mmol), the reaction mixture was stirred for 72 h. The crude product was purified by column chromatography (EtOAc/hexanes 2/8) to provide an inseparable mixture of cycloadducts **29b** and **30b** (66.3 mg, 0.174 mmol, 92%, dr = 56:44 measured by ^1H NMR) as a yellow oil: R_f = 0.60 (EtOAc/hexanes

2/8); IR (neat, NaCl) 3461, 2954, 2870, 2859, 1710, 1646, 1472 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 4.16 (q, 0.88H, J = 7.2 Hz), 4.15 (q, 1.12H, J = 7.1 Hz), 3.81−3.89 (m, 1H), 3.54−3.62 (m, 1H), 3.47−3.52 (m, 1H), 2.60−2.64 (m, 1H), 2.58 (br s, 1H), 2.46−2.48 (m, 1H), 2.45−2.46 (m, 1H), 2.41−2.43 (m, 0.44H), 2.16 (br s, 0.56H), 2.03−2.06 (m, 1H), 1.54−1.57 (m, 2H), 1.27 (t, 3H, J = 7.1 Hz), 1.05−1.08 (m, 2H), 0.98−1.00 (m, 1H), 0.893 (s, 5.04H), 0.891 (s, 3.96H), 0.87−0.88 (m, 1H), 0.063 (s, 3.36H), 0.059 (s, 2.64H); ^{13}C NMR (APT, $CDCl_3$, 75 MHz) major isomer δ 163.2, 160.3, 132.3, 70.0, 67.1, 59.8, 49.0, 46.36, 33.9, 33.5, 33.1, 30.6, 28.1, 27.9, 25.9, 18.3, 14.3, −5.4, visible peaks for minor isomer δ 163.4, 160.4, 132.1, 70.3, 67.0, 59.7, 49.4, 46.41, 33.6, 33.2; HRCI calcd for $C_{21}H_{36}O_4Si$ $[M + H]^+$ 381.2465, found 381.2461.

Cycloadducts 29c and 30c (Table 4, Entry 3). Following the above general procedure with norbornene **1** (47.5 mg, 0.504 mmol), homopropargylic alcohol **27c** (35.3 mg, 0.162 mmol), THF (0.30 mL), and Cp*RuCl(COD) (8.6 mg, 0.023 mmol), the reaction mixture was stirred for 72 h. The crude product was purified by column chromatography (EtOAc/hexanes 2/8) to provide an inseparable mixture of cycloadducts **29c** and **30c** (44.6 mg, 0.143 mmol, 89%, dr = 72:28 measured by ^1H NMR) as a yellow oil: R_f = 0.50 (EtOAc/hexanes 2/8); IR (neat, NaCl) 3418, 2952, 2871, 1712, 1694, 1682, 1650, 1454, 1370 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.24−7.40 (m, 5H), 4.91−4.97 (m, 1H), 4.19 (q, 2H J = 7.1 Hz), 3.49 (br s, 1H), 2.93−2.99 (m, 1H), 2.72−2.85 (m, 1H), 2.62 (d, 0.28H, J = 3.8 Hz), 2.59 (d, 0.72H, J = 3.3 Hz), 2.56 (d, 0.28H, J = 3.0 Hz), 2.38 (d, 0.72H, J = 2.8 Hz), 2.26 (d, 0.28H, J = 3.1 Hz), 2.16 (br s, 0.72H), 2.03 (br s, 0.28H), 1.93 (br s, 0.72H), 1.49−1.60 (m, 2H), 1.30 (t, 3H, J = 7.1 Hz), 1.19−1.22 (m, 1H), 0.93−1.10 (m, 3H); ^{13}C NMR (APT, $CDCl_3$, 75 MHz) major isomer δ 163.6, 160.3, 144.3, 132.6, 128.4, 127.5, 125.7, 72.1, 60.0, 48.8, 46.4, 39.5, 33.8, 33.3, 30.5, 28.0, 27.8, 14.3, visible peaks for minor isomer δ 163.7, 160.4, 132.5, 127.4, 125.5, 72.4, 49.6, 39.6, 33.9, 33.5; HRCI calcd for $C_{20}H_{24}O_3$ $[M + H]^+$ 313.1806, found 313.1804.

■ ASSOCIATED CONTENT

Supporting Information

Text and figures giving ^1H and ^{13}C NMR spectra of all new compounds and details of the preparation and characterization of alkynes. 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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