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Ruthenium(II)-Catalyzed [2+2] Cycloadditions of *anti* 7-Substituted Norbornenes

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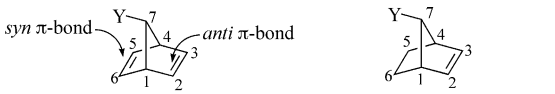
The ruthenium(II)-catalyzed [2+2] cycloadditions of *anti* 7-substituted norbornenes with an alkyne were investigated. The cycloadditions were found to proceed with a high degree of stereoselectivity, giving only the *exo* stereoisomers in moderate to good yields using an improved protocol. Comparative rate studies between a variety of *anti* 7-substituted norbornenes and an alkyne revealed that the reactivity of the alkene component decreases dramatically as the alkene becomes more electron deficient.

Introduction

The synthesis of cyclobutene derivatives has recently been accomplished through transition-metal-mediated strategies.[1,2] In particular, metal-catalyzed [2+2] cycloadditions between an alkene and alkyne serve as an important pathway to these targets.[3–8] Although a thermally forbidden process according to the Woodward–Hoffmann rules,[9] [2+2] cycloadditions can also be accomplished by photochemical means,[10] by way of thermal reactions proceeding through biradical intermediates,[11] and by the incorporation of Lewis acid catalysts.[12] Over the last decade significant advances have been made regarding transition metal-catalyzed [2+2] cycloadditions of alkenes with alkynes, but many questions remain unanswered at this time.

Several years ago we initiated a research program concerned with synthesizing a variety of cyclobutene targets that would serve as useful precursors in the development of larger molecules. In order to fully exploit Ru^{II}-catalyzed [2+2] cycloadditions, it is necessary to develop a better understanding of the mechanism and stereoelectronic environment associated with this reaction. For this reason, several comparative rate studies that would provide some insight into the reactivity of the alkene and alkyne components associated with a Ru^{II}-catalyzed [2+2] cycloaddition were undertaken.[8b,8k] In our initial competitive rate study we reported on the reactivity of 7-substituted norbornadienes (NBDs) **1a**–**f** in Ru^{II}-catalyzed [2+2] cycloadditions (Figure 1).[8b] C-7-Substituted NBDs were selected as the model compounds as they were known from literature to perturb the electron density of the *anti* π-bond (*anti* and *syn* are used to describe the relationship between the Y substituents and π-bonds), thus influencing their reactivity.[13] At this stage, we were satisfied that this phenomenon allowed us to probe the electronic environment associated with the alkene component. A conclusion was made from these preliminary findings that electron-deficient alkenes appeared to react much slower in Ru^{II}-catalyzed [2+2] cycloadditions. Generally speaking, aryl and alkyl groups reacted much faster. However, at the completion of this study several questions evolved concerning the observed relative rate differences. Were the observed relatives rates a reflection of the through-space interaction between the 7-substituent and the *anti* π-bond as was believed? Was the possible bidentate nature of the 7-substituted NBDs influencing the reactivity of the alkenes? And finally, was there an interaction between the 7-substituent and the *syn* π-bond of NBD that was influencing the *anti* π-bond and thus controlling the reactivity? With these questions in mind, we designed a comparative rate study that would utilize *anti* 7-substituted norbornenes (NBNs) **2** to address the aforementioned con-



7-substituted norbornadienes

1a: Y = H
b: Y = O*t*Bu
c: Y = OAc
d: Y = OTBDMS
e: Y = Hexyl
f: Ph

anti 7-substituted norbornenes

2a: Y = OTBDMS
b: Y = OAc
c: Y = O*t*Bu
d: Y = H
e: Y = Ph

Figure 1. 7-Substituted norbornadienes and *anti* 7-substituted norbornenes.

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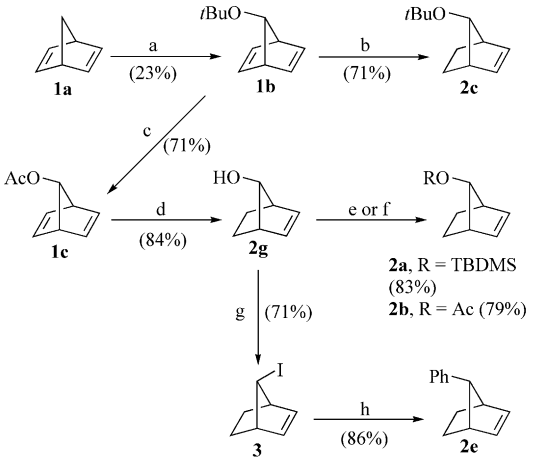
cerns and our findings are discussed within this paper. The use of *anti* 7-substituted NBNs eliminates the possibility of homoconjugation as well as a bidentate binding mode. However, an electronic interaction between the C7-substituent and the *anti* π-bond should remain. We were primarily concerned with verifying our conclusions concerning the electronic environment of the alkene component as it relates to Ru^{II}-catalyzed [2+2] cycloadditions.

Results and Discussion

In order to answer the above questions we needed to access a variety of *anti* 7-substituted NBNs. The synthesis of our required substrates was, for the most part, possible through the application of known protocols from the literature.[14] It was found that starting from commercially available NBD **1a** allowed access to the desired substrates as shown in Scheme 1. The synthesis of these materials proceeded smoothly in most cases.[15] However, in the case of *anti* 7-PhNBN **2e** a greater deal of resilience was required. Numerous nucleophiles (cuprates and lithiated species) and leaving groups (tosylate, mesylate and alkoxy moieties) were screened in an exhaustive attempt to obtain this NBN. This target was finally realized with the combination of a Grignard reagent and *syn* 7-IodoNBN **3**.

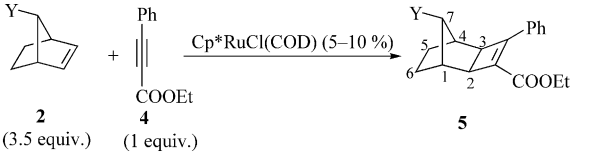


Reagents: (a) *tert*-Butyl peroxybenzoate, CuBr; (b) LAH; (c) Ac_2O, AcOH, $HClO_4$; (d) LAH; (e) TBDMSCl, imidazole; (f) Ac_2O, pyridine, DMAP; (g) Ph_3P, I_2, imidazole; (h) PhMgBr

Scheme 1. Synthesis of *anti* 7-substituted norbornenes.

With the starting materials in hand, it was then necessary to develop some conditions for the Ru-catalyzed [2+2] cycloadditions to proceed. In our initial optimization experiments we loosely followed the conditions of the Ru-catalyzed [2+2] cycloadditions developed previously in our research group.[8] However, under these reaction conditions, the cycloadducts were obatined in very low to moderate yields (Table 1, Entries 1–3, 5, 7). Alteration of reaction variables such as solvent, temperature, and molar equivalencies at best provided only minor enhancements in the yields. After careful consideration, it was put forward that the order in which the reagents were combined could influence the reactivity. Up until this point, our protocols involved combining the reagents with the catalyst in one step (Table 1, method A). This idea was easily tested with a procedure that employed premixing the alkenes **2a**–**e** and Cp*RuCl(COD) followed by the slow addition of the alkyne **4** (Table 1, method B). Much to our delight, using this new procedure, we were now able to obtain the cycloadducts in good yields. Our improved protocol significantly enhances the yields of the cycloadditions (Table 1, Entries 4, 6, 8 and 10). However, to obtain good yields for cycloadducts **5a** and **5b** (Y = OTBDMS and Y = OAc), a higher catalyst loading of 15 mol-% was required due to their poor reactivity (for alkenes **2c**–**2e**, Table 1, Entries 7–12, catalyst loading of 5–10 mol-% was used). In accordance with our previous findings, the cycloadditions occurred exclusively on the *exo* face of the bicyclic framework, once again imparting a high degree of stereoselectivity.[16]

Table 1. Optimization of reaction conditions for Ru^{II}-catalyzed [2+2] cycloadditions of a*nti* 7-substituted norbornenes **2a**–**e**.



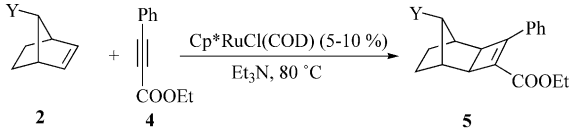
Entry	NBN	Y	Cycloadduct	Method[a]/solv./temp./time	Yield (%)[b]
1	**2a**	OTBDMS	**5a**	A/Et_3N/80 °C/89 h	16[c]
2	**2a**	OTBDMS	**5a**	A/Et_3N/80 °C/7 d	21[c]
3	**2a**	OTBDMS	**5a**	A/Et_3N/80 °C/112 h	37[c]
4	**2a**	OTBDMS	**5a**	B/Et_3N/70 °C/5 h	82[d]
5	**2b**	OAc	**5b**	A/Et_3N/90 °C/138 h	<5[c]
6	**2b**	OAc	**5b**	B/Et_3N/90 °C/25 h	71[d]
7	**2c**	O*t*Bu	**5c**	A/Et_3N/90 °C/7 d	62[c]
8	**2c**	O*t*Bu	**5c**	B/THF/60 °C/3 h	90
9	**2d**	H	**5d**	A/THF/60 °C/19 h	89
10	**2d**	H	**5d**	B/THF/60 °C/3 h	95
11	**2e**	Ph	**5e**	A/THF/60 °C/22 h	98
12	**2e**	Ph	**5e**	B/THF/60 °C/3 h	90

[a] Method A: combined 7-NBN compounds **2a**–**e** and the alkyne **4** with Cp*RuCl(COD) in one step. Method B: premixed 7-NBN compounds **2a**–**e** and Cp*RuCl(COD) first followed by slow addition of the alkyne **4**. [b] Isolated yields after column chromatography. [c] 30–90% of the unreacted alkyne **4** was recovered. [d] 15 mol-% of Cp*RuCl(COD) was used.

In order to address the questions raised, some comparative rate experiments were conducted. The reactivity of the *anti* 7-substituted norbornenes were investigated. Each relative rate experiment involved the use of an equimolar amount of the two alkenes under comparison. The alkenes **2a**–**e** being studied are in excess (6 equiv.) relative to the alkyne **4** (1 equiv.) so that *pseudo*-first-order conditions prevail.[17] Under these conditions we were able to compare the product ratios by careful GLC analysis.[18] During our optimization experiments it was realized that *anti* 7-OAcNBN **2b** was, qualitatively speaking, the least reactive alkene and would therefore serve as a good benchmark. The relative rate differences between *anti* 7-OAcNBN **2b** and the

remaining *anti* 7-NBNs **2a**, **c**–**e** obtained in this study are outlined in Table 2. The data clearly shows an impressive rate enhancement when Y = Ph (40-fold increase) and Y = H (29-fold increase). However, the silyloxy NBN **2a** (5-fold increase) and alkoxy NBN **2c** (6-fold increase) only yielded moderate differences.

Table 2. Relative rate of Ru^{II}-catalyzed [2+2] cycloadditions of *anti* 7-substituted norbornenes.



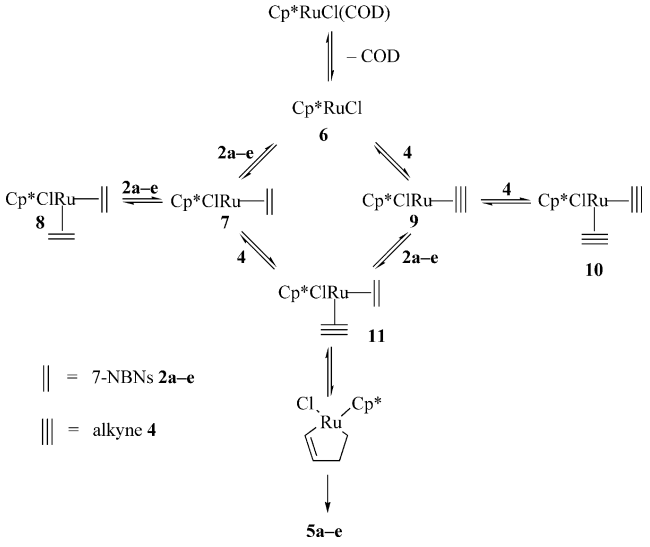
2 (6 equiv.) **4** (1 equiv.) **5** *anti-exo*

Entry	Norbornene	Y	Cycloadduct	Relative rate[a]
1	**2b**	OAc	**5b**	1
2	**2a**	OTBS	**5a**	5
3	**2c**	O*t*Bu	**5c**	6
4	**2d**	H	**5d**	29
5	**2e**	Ph	**5e**	40

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

At first glance, it would appear that an EWG would suppress the reactivity of the alkene component in Ru^{II}-catalyzed [2+2] cycloadditions. However, a Ph group would typically be classified as a weak EWG (inductively speaking). We have yet to find irrefutable evidence for explaining the reactivity of **2e** and at this point we can only speculate. We believe the enhanced reactivity could in fact be attributed to a significant through-space interaction between the Ph group and the *anti* π-bond or a bond distortion in the bicyclic framework, which leads to an increase in electron density on the *anti* π-bond thus altering the reactivity. This increased electron density could significantly enhance the ability of **2e** to bind to the metal thus making it more reactive. This increased reactivity could, to some degree, be attributed to a difference in strain energies. It is important to note that the relative rate differences observed for this study were nearly identical to those observed with 7-substituted NBDs **1a**–**f**.[8b] In fact, the order of reactivity was identical (Ph > H > O*t*Bu > OTBDMS > OAc) for both studies. If the metal was interacting in a bidentate fashion with the 7-NBDs previously studied, it would be expected that the observed relative rate differences and order would, to some degree, reflect this behaviour. However, the nearly identical data obtained in both studies suggests otherwise. These results also dismiss the idea that the C-7 substituents were altering the electron density of the *anti* π-bond via a through-space interaction with the *syn* π-bond. For example, a π-stacking or π-π-orbital interaction between the *syn* π-bond and Ph substituent is most likely not responsible for the enhanced reactivity of 7-PhNBD **1f**. If this was the controlling interaction, one might have expected to see a different reactivity pattern in the 7-NBN series due to the absence of a *syn* π-bond. We believe the observed trends support the idea that the differences in reactivity reflect an electronic interaction of the C-7 substituents and the *anti* π-bond.

The development of our improved protocol of the Ru-catalyzed [2+2] cycoaddition and its effects warrants further discussion. A brief overview of the proposed reaction mechanism provides a plausible explanation for this increased reactivity (Scheme 2). The proposed catalytic cycle begins through dissociation of the weakly bound COD ligand from Cp*RuCl(COD) (18-electron complex), leading to the formation of the neutral species Cp*RuCl (**6**). Trapping of this 14-electron intermediate can proceed in several fashions. For instance, the interception of **6** with one molecule of 7-NBN **2a**–**e** leads to the formation of intermediate **7**, while the complexation of one molecule of alkyne **4** results in the formation of **9**. In the event that alkyne **4** intercepts intermediate **7** or alkenes **2a**–**e** capture intermediate **9** the formation of intermediate **11** would result. At this point, the stage would be set for the desired catalytic pathway. However, in the event that two alkyne molecules have become bound to the catalyst, an inactive, saturated catalyst **10** would result.[19] On the other hand, coordination of two 7-NBN molecules would produce coordinatively saturated complex **8**. These last two pathways are unfavourable as they would prevent or slow the desired catalytic route. If the pathway leading to **8** was detrimental to the reaction, then our modified procedure (Table 1, method B) would surely poison the catalyst. On the contrary, the reaction proceeds with ease, suggesting that the equilibrium between **7** and **8** is either fast or lies in the direction of **7**. Alkenes **2a**–**e** must be weakly bound to the metal and exchange easily with alkyne **4**. We believe that in the case of 7-NBNs **2a**–**e**, the competitive complexation pathway leading to **10** plays an important role. The greater affinity of the metal towards the alkyne **4** would allow the association/dissociation equilibrium to lie largely in the direction of the undesired coordinatively saturated species **10**.



Scheme 2. The proposed mechanism for a Ru^{II}-catalyzed [2+2] cycloaddition.

Inclusion of a premixing step was formulated to help overcome the perceived problem associated with the inability of the 7-NBN compounds **2a**–**e** to complex to the metal. Introduction of the weaker binding alkenes prior to the alkyne **4** permits complexation of the alkenes first, allowing us to "bias" the reaction in our favour. Under these conditions the formation of intermediates **7** and **8** would predominant. The alkyne **4** was then slowly introduced to the reaction in a fashion so as to allow the cycloaddition to occur. As the alkyne **4** was introduced, a ligand exchange would have occurred leading to **11**. If the introduction of the alkyne **4** proceeds too quickly a double ligand exhange would most likely occur, thus leading to the intermediate **10**. It is important to realize that at any given time, only a small percentage of the alkene is complexed to the metal due to the catalytic amount of Cp*RuCl(COD) used relative to the amount remaining in solution. Therefore, in order to maintain a system in which the desired catalytic cycle operates, the alkyne **4** must be introduced carefully so as to minimize the saturation of the active catalytic species. Exclusion of the intermediate **10** from the catalytic process appears to enhance the reaction. By increasing the probability of forming **11** we could be driving the equilibrium between **11** and the oxidative addition product in our favour, thus increasing the formation of our cycloadducts. However, when using our previous procedure (Table 1, method A), the formation of **10** must have been a dominate pre-equilibrium that was ultimately poisoning the desired catalytic pathway.

Conclusions

In conclusion, our findings from this study have allowed us to confirm our preliminary conclusions relating to our comparative rate experiments dealing with 7-NBDs **1a**–**f**. We have demonstrated that the trend in reactivity for the 7-NBDs **1a**–**f** was not related to the *syn* π-bond or the bidentate nature of NBDs but was most likely the result of an interaction between the C-7 substituent and the *anti* π-bond. Furthermore, we have shown through comparative rate studies that electron deficient 7-NBNs react slower in Ru^{II}-catalyzed [2+2] cycloadditions. During the course of this investigation we have also developed an improved procedure that was highlighted by lower reaction times, temperatures, and good to excellent yields.

Experimental Section

General Information: RBF = round-bottom flask. 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) using flash column chromatography techniques.[20] Analytical thin-layer chromatography (TLC) was performed on Merck precoated silica gel 60 F_{254} plates. All glassware was flame dried under dry nitrogen. Infrared spectra were taken with a Bomem MB-100 FTIR spectrophotometer. ^1H and ^{13}C NMR spectra were recorded with a Bruker Avance-400 spectrometer. Chemical shifts for ^1H 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 done 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. GC analyses were performed using 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, air flow rate: 450 mL/min

Materials: Unless stated otherwise, commercial reagents were used without purification. The solvents were purified by distillation under dry nitrogen, from CaH_2 (Et_3N) and from potassium/benzophenone (THF). The 7-substituted norbornadienes **1b**–**c**,[14] Cp*RuCl(COD)[21] and the alkyne **4**[22] were prepared according to literature procedures.

***anti*-7-*tert*-Butoxybicyclo[2.2.1]hept-2-ene (2c):** Lithium aluminum hydride (0.550 g, 14.5 mmol) was weighed directly into a flame-dried flask and cooled to 0 °C before adding THF (12.0 mL). Norbornadiene **1b**[14] (0.427 g, 2.60 mmol) in THF (1.0 mL) was transferred at 0 °C by a cannula to the reaction mixture. The reaction was stirred at 0 °C for 5 min and then warmed to room temp. before heating to reflux. The mixture was stirred for 64 h at reflux. At this point the reaction mixture was cooled to 0 °C and quenched extremely slow due to the large excess of lithium aluminum hydride present. Water (0.40 mL), 3 M NaOH (0.4 mL), and water (1.3 mL) were sequentially used to quench the reaction. The crude mixture was stirred at room temp. for 20 min and boiled for 15 min to ensure precipitation of the aluminum salt byproducts. The crude product was filtered through a sintered glass funnel containing a plug of silica to remove the white precipitate and washed with Et_2O. After the solvent was removed via rotary evaporation, the crude product was purified by column chromatography (EtOAc/hexanes, 0:1, 1:19) to give the norbornene **2c** (0.306 mg, 1.84 mmol, 71%) as colourless liquid. R_f = 0.47 (EtOAc/hexanes, 1:19). ^1H NMR ($CDCl_3$, 400 MHz): δ = 5.97 (dd, J = 2.2, 2.1 Hz, 2 H), 3.30 (br. s, 1 H), 2.44 (d, J = 1.5 Hz, 2 H), 1.81 (m, 2 H), 1.15 (s, 9 H), 0.90 (dd, J = 10.4, 3.8 Hz, 2 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 134.3, 83.1, 73.0, 45.8, 28.5, 22.0 ppm. This is a known compound in the literature.[14]

***anti*-Bicyclo[2.2.1]hept-2-en-7-ol (2g):** Et_2O (15 mL) was added to a flame-dried flask containing lithium aluminum hydride (0.205 g, 5.40 mmol) at 0 °C. A solution containing norbornadiene **1c**[14] (0.508 g, 3.38 mmol) in Et_2O (2 mL) was transferred dropwise via a cannula to the above suspension at 0 °C. The mixture was stirred at 0 °C for 5 min and for 2 h at room temp. At this time, the solution was cooled back down to 0 °C and quenched carefully with saturated Na_2SO_4. The crude mixture was filtered through a sintered glass funnel containing a plug of silica with Et_2O. The crude mixture was carefully concentrated (the product sublimes easily) by rotary evaporation and purified by column chromatography (Et_2O-:pentanes, 2:3) to give the norbornene **2g** (0.313 g, 2.84 mmol, 84%) as a white solid. R_f = 0.25 (EtOAc/hexanes, 1:4). ^1H NMR ($CDCl_3$, 400 MHz): δ = 5.96 (dd, J = 2.2, 2.1 Hz, 2 H), 3.56 (br. s, 1 H), 2.53 (m, 2 H), 1.80 (m, 2 H), 1.79 (br. s, 1 H), 1.02 (dd, J = 10.9, 3.9 Hz, 2 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 134.5, 82.4, 45.5, 21.3 ppm. This is a known compound in the literature.[14]

***anti*-(Bicyclo[2.2.1]hept-2-en-7-yloxy)-*tert*-butyldimethylsilane (2a):** DMF (6.0 mL) was added in a flame-dried flask containing norbornene **2g** (0.742 g, 6.74 mmol). Imidazole (0.713 g, 10.5 mmol) and TBDMSCl (1.38 g, 9.14 mmol) were sequentially introduced as solids at room temp. The reaction mixture was stirred at room temp. for 4 h before being quenched with water. The crude mixture was diluted with 20 mL of 10% CH_2Cl_2/hexanes before extraction. The organic product was then extracted into 10% CH_2Cl_2/hexanes and washed with water and brine. The crude mixture was evaporated to dryness after drying over $MgSO_4$ and filtration. The crude product was purified by column chromatography (EtOAc/hexanes, 0:1, 1:19) to give the norbornene **2a** (1.25 g, 5.59 mmol, 83%) as a colourless liquid. R_f = 0.65 (EtOAc/hexanes, 1:19). IR (neat): $\tilde{\nu}_{max}$ = 3061 (w), 2956 (s), 2859 (m), 1708 (w), 1682 (w), 1472 (w), 1361 (w), 1303 (w), 1257 (m), 1130 (s), 1113 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 5.94 (dd, J = 2.3, 2.1 Hz, 2 H), 3.43 (br. s, 1 H), 2.42 (m, 2 H), 1.80 (m, 2 H), 0.91 (dd, J = 10.6, 3.8 Hz, 2 H), 0.87 (s, 9 H), 0.02 (s, 6 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 134.1, 82.7, 46.2, 25.7, 21.7, 17.9, –4.8 ppm. HRMS calcd. for $C_{13}H_{24}OSi$: m/z 224.1596, found m/z 224.1597.

***anti*-7-Acetoxybicyclo[2.2.1]hept-2-ene (2b):** This is a known compound in the literature.[23] CH_2Cl_2 (3.0 mL) was added in a flame-dried flask containing the norbornene **2g** (337 mg, 3.06 mmol). Pyridine (0.73 mL, 9.0 mmol), Ac_2O (0.42 mL, 4.5 mmol), and DMAP (16.1 mg, 0.130 mmol) were added sequentially to the solution at room temp. The reaction mixture was stirred for 19 h at room temp. before quenching with water. The crude product was extracted from the aqueous layer with CH_2Cl_2. The combined organic layers were washed with a solution of saturated $CuSO_4$, water and brine. This was then followed up with drying over $MgSO_4$ and filtration. The crude mixture was evaporated to dryness and purified by column chromatography (EtOAc/hexanes, 0:1, 1:19) to afford the norbornene **2b** (0.366 g, 2.40 mmol, 79%) as a colourless liquid. R_f = 0.43 (EtOAc/hexanes, 1:19). ^1H NMR ($CDCl_3$, 400 MHz): δ = 6.00 (dd, J = 2.3, 2.1 Hz, 2 H), 4.30 (br. s, 1 H), 2.74 (m, 2 H), 2.01 (s, 3 H), 1.74 (m, 2 H), 1.03 (m, 2 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 170.7, 133.9, 82.6, 43.3, 21.7, 21.2 ppm.

***syn*-7-Iodobicyclo[2.2.1]hept-2-ene (3):** This is a known compound in the literature.[24] A mixture of THF (16.0 mL) and CH_3CN (63.0 mL) was added to a flame-dried flask containing PPh_3 (9.54 mg, 36.4 mmol) and imidazole (5.27 mg, 77.4 mmol). Iodine (9.22 mg, 72.6 mmol) was then added in one portion as a solid to the mixture at 0 °C. The red-brown mixture was stirred at 0 °C for 15 min. A solution of **2g** in CH_3CN was transferred to the above RBF via a cannula at 0 °C. The reaction was stirred at 0 °C for 15 min and at room temp. for 90 min at which time a white precipitate evolved. The crude mixture was quenched with water and diluted with hexanes. The organic product was extracted from the aqueous layer using 10% CH_2Cl_2/hexanes. The combined organic layers were washed with a solution of saturated NaS_2O_3, water, and brine before drying over Na_2SO_4 and filtration. The crude product was filtered through a sintered glass funnel containing a plug of silica with hexanes to give **3** (2.85 g, 13.0 mmol, 71%) as a colourless liquid. R_f = 0.62 (pentane). ^1H NMR ($CDCl_3$, 400 MHz): δ = 6.01 (dd, J = 2.1, 2.0 Hz, 2 H), 3.86 (t, J = 1.5 Hz, 1 H), 2.87 (d, J = 1.5 Hz, 2 H), 2.13 (m, 2 H), 1.14 (m, 2 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 135.1, 48.5, 39.5, 22.3 ppm.

***anti*-7-Phenylbicyclo[2.2.1]hept-2-ene (2e):** In a flame-dried 100-mL 3-necked RBF containing Mg (0.109 g, 4.56 mmol) was charged with Et_2O (12.0 mL) and dibromoethane (0.01 mL, 0.12 mmol). Bromobenzene (0.48 mL, 4.6 mmol) was then added in 2 portions. The first portion of bromobenzene (0.24 mL) was added and the solution was stirred for 15 min after which time the solution became milky. The remaining bromobenzene was then added slowly. Upon completion of the addition, the solution was refluxed until the Mg was consumed (1 h 15 min). The freshly prepared Grignard reagent was added to a flame-dried flask containing toluene (4.5 mL). The Et_2O was then removed by distillation and the reaction mixture was charged with additional toluene (3.0 mL). *syn*-7-Iodobicyclo[2.2.1]hept-2-ene (**3**) (0.399 g, 1.81 mmol), diluted in toluene (0.5 mL), was transferred at this time to the grignard reagent through a cannula at room temp. The residue was rinsed with toluene (2 × 0.5 mL) and transferred to the reaction mixture. The reaction mixture was then heated to 80 °C for 27 h. The yellow solution produced a white precipitate upon heating. The reaction was quenched sequentially with water and 1 M HCl and stirred for 15 min at room temp. The aqueous layer was extracted with hexanes. The combined organic layers were washed with water and brine followed by drying over $MgSO_4$ and filtration. Upon removal of the solvent via rotatary evaporation, the crude product was purified by column chromatography (EtOAc/hexanes, 0:1) to give norbornene **2e** (0.264 g, 1.55 mmol, 86%) as a colourless liquid. R_f = 0.35 (EtOAc/hexanes, 0:1). IR (neat): $\tilde{\nu}_{max}$ = 3059 (s), 3027 (s), 2967 (s), 2905 (m), 2871 (m), 1944 (w), 1878 (w), 1802 (w), 1748 (w), 1709 (w), 1684 (w), 1638 (w), 1602 (m), 1496 (s), 1448 (s), 1327 (s), 1127 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.29 (d, J = 6.8 Hz, 2 H), 7.19 (m, 3 H), 6.21 (app t, J = 1.9 Hz, 2 H), 3.18 (m, 2 H), 2.84 (br. s, 1 H), 1.51 (m, 2 H), 0.95 (m, 2 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 141.2, 136.6, 128.2, 126.9, 125.6, 61.4, 43.9, 21.9 ppm. HRMS calcd. for $C_{13}H_{14}$: m/z 170.1096, found m/z 170.1090.

General Procedure (B) for Ruthenium-Catalyzed [2+2] Cycloadditions: The bicyclic alkene **2** (0.35 mmol, 3.5 equiv.), diluted in THF or Et_3N (0.05 mL), was transferred through a cannula to an oven-dried screw-cap vial containing Cp*RuCl(COD) (weighed out from a dry box, 0.01 mmol, 10 mol-%) under nitrogen. The solution was stirred in the darkness for 25–35 min at 60–85 °C. The acetylene **4** (0.1 mmol, 1 equiv.), diluted in THF or Et_3N (0.06 mL), was then added dropwise over a 50–115 min to the above solution at 60–85 °C. The reaction was stirred for an additional 1.5–23 h at 60–85 °C. The reaction was monitored by TLC analysis. The crude product was purified by column chromatography (EtOAc/hexanes mixtures) to give the cycloadduct.

Cycloadduct 5a. General Method B: (Table 1, Entry 4). Norbornene **2a** (49.6 mg, 0.221 mmol), acetylene **4** (11.9 mg, 0.068 mmol), Et_3N (0.06 + 0.06 mL), Cp*RuCl(COD) (4.3 mg, 0.011 mmol) were used. The solution was stirred in the darkness for 30 min at 70 °C. The alkyne **4** was added over a 1 h at 70 °C. The reaction was stirred for an additional 4 h at 70 °C. The crude product was purified by column chromatography (EtOAc/hexanes, 0:1, 3:97, 1:9) to give the cycloadduct **5a** (22.2 mg, 0.056 mmol, 82%) as a white solid. R_f = 0.35 (EtOAc/hexanes, 1:19); m.p. 68.5–69 °C. GC (HP-1 column): retention time 18.961 min. IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 2956 (s), 2858 (m), 1705 (s), 1615 (m), 1463 (m), 1250 (m), 1216 (s), 1196 (s), 1127 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.01 (m, 2 H), 7.38 (m, 3 H), 4.26 (m_{ABX}, 2 H), 3.98 (s, 1 H), 2.86 (d, J = 4.0 Hz, 1 H), 2.77 (d, J = 4.0 Hz, 1 H), 2.14 (br. s, 1 H), 2.10 (br. s, 1 H), 1.94 (dd, J = 9.7, 3.0 Hz, 2 H), 1.34 (t, J = 7.1 Hz, 3 H), 1.19 (d, J = 9.7 Hz, 2 H), 0.81 (s, 9 H), –0.06 (s, 3 H), –0.09 (s, 3 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 162.9, 155.2, 132.5, 130.0, 128.8, 128.3, 128.1, 76.0, 60.0, 45.8, 45.3, 39.4, 38.8, 26.3, 26.2, 25.7, 18.0, 14.4, –4.88, –4.93 ppm. HRCI calcd. for $C_{24}H_{35}O_3Si$: $[m + H]/z$ 399.2355, found $[m + H]/z$ 399.2345.

Cycloadduct 5b. General Method B: (Table 1, Entry 6). Norbornene **2b** (82.4 mg, 0.541 mmol), acetylene **4** (20.0 mg, 0.115 mmol), Et_3N (0.10 + 0.05 mL), Cp*RuCl(COD) (7.2 mg, 0.019 mmol) were used. The solution was stirred in the darkness for 35 min at 85 °C. Alkyne **4** was added over an 2 h at 85 °C. The reaction was stirred for an additional 23 h min at 85 °C. The crude product was purified by column chromatography (EtOAc/hexanes, 0:1, 1:19, 1:9) to give the cycloadduct **5b** (26.5 mg, 0.081 mmol, 71%) as a white solid. R_f = 0.23 (EtOAc/hexanes, 1:9); m.p. 84–85.5 °C. GC (HP-1 column): retention time 18.379 min. IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 3065 (m), 2973 (s), 2876 (m), 1738 (s), 1703 (s), 1615 (m), 1492 (m), 1367 (m), 1246 (s), 1220 (s), 1199 (s), 1078 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.02 (m, 2 H), 7.38 (m, 3 H), 4.85 (s, 1 H), 4.26 (m_{ABX}, 3 H), 2.93 (d, J = 4.0 Hz, 1 H), 2.84 (d, J = 4.0 Hz, 1 H), 2.47 (br. s, 1 H), 2.43 (br. s, 1 H), 1.99 (s, 3 H), 1.88 (dd, J = 10.1, 3.2 Hz, 2 H), 1.34 (t, J = 7.1 Hz, 3 H), 1.32 (d, J = 10.1 Hz, 2 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 170.6, 162.6, 154.9, 132.2, 130.2, 128.9, 128.4, 128.1, 79.1, 60.2, 45.4, 44.9, 37.1, 36.7, 26.2, 26.1, 21.1, 14.3 ppm. $C_{20}H_{22}O_4$: C 73.60, H 6.79; found C 73.44, H 6.89.

Cycloadduct 5c. General Method B: (Table 1, Entry 8). Norbornene **2c** (86.5 mg, 0.520 mmol), acetylene **4** (20.5 mg, 0.118 mmol), THF (0.05 + 0.06 mL), Cp*RuCl(COD) (5.1 mg, 0.013 mmol) were used. The solution was stirred in the darkness for 30 min at 60 °C. The alkyne **4** was added over a 1 h 60 °C. The reaction was stirred for an additional 2 h at 60 °C. The crude product was purified by column chromatography (EtOAc/hexanes, 0:1, 1:19) to give the cycloadduct **5c** (36.1 mg, 0.106 mmol, 90%) as a white solid. R_f = 0.43 (EtOAc/hexanes, 1:9); m.p. 95–95.5 °C. GC (HP-1 column): retention time 17.127 min. IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 3056 (m), 2975 (s), 2872 (w), 1701 (s), 1615 (m), 1447 (m), 1265 (s), 1197 (m), 1111 (w) cm-1 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.03 (m, 2 H), 7.38 (m, 3 H), 4.26 (m_{ABX}, 2 H), 3.82 (s, 1 H), 2.82 (d, J = 3.9 Hz, 1 H), 2.74 (d, J = 3.9 Hz, 1 H), 2.15 (s, 1 H), 2.10 (s, 1 H), 1.94 (dm, J = 9.4 Hz, 2 H), 1.33 (t, J = 7.1 Hz, 3 H), 1.18 (dm, J = 8.4 Hz, 2 H), 1.06 (s, 9 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 162.9, 155.3, 132.6, 129.9, 128.8, 128.4, 128.2, 75.2, 73.0, 60.0, 45.7, 45.2, 39.0, 38.4, 28.4, 26.6, 26.5, 14.4 ppm. $C_{22}H_{28}O_3$: C 77.61, H 8.29; found C 77.48, H 8.38.

Cycloadduct 5d. General Procedure B: (Table 1, Entry 10). Norbornene **2d** (36.6 mg, 0.389 mmol), acetylene **4** (19.9 mg, 0.114 mmol), THF (0.06 + 0.06 mL), Cp*RuCl(COD) (2.9 mg, 0.008 mmol) were used. The solution was stirred in the darkness for 35 min at 60 °C. Alkyne **4** was added over 45 min at 60 °C. The reaction was stirred for an additional 2 h 15 min at 60 °C. The crude product was purified by column chromatography (EtOAc/hexanes, 0:1, 1:19) to give the cycloadduct **5d** (29.1 mg, 0.108 mmol, 95%) as colourless oil. R_f = 0.33 (EtOAc/hexanes, 1:19). GC (HP-1 column): retention time 15.958 min. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.03 (m, 2 H), 7.37 (m, 3 H), 4.25 (m_{ABX}, 2 H), 2.80 (d, J = 3.6 Hz, 1 H), 2.70 (d, J = 3.6 Hz, 1 H), 2.27 (d, J = 1.1 Hz, 1 H), 2.24 (d, J = 1.1 Hz, 1 H), 1.63 (m, 2 H),1.40 (dm, J = 10.4 Hz, 1 H), 1.34 (t, J = 7.1 Hz, 3 H), 1.20 (m, 2 H), 1.04 (dt, J = 10.4, 1.1 Hz, 1 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 163.1, 155.6, 132.7, 129.8, 128.8, 128.7, 128.3, 59.9, 46.5, 46.0, 34.7, 34.2, 30.6, 28.33, 28.32, 14.3 ppm. This is a known compound in the literature.[3c]

Cycloadduct 5e. General Method B: (Table 1, Entry 12). Norbornene **2e** (58.7 mg, 0.345 mmol), acetylene **4** (16.7 mg, 0.096 mmol), THF (0.05 + 0.06 mL), and Cp*RuCl(COD) (3.4 mg, 0.009 mmol) were used. The solution was premixed in the darkness for 25 min at 60 °C. Alkyne **4** was added over a 1 h at 60 °C. The reaction was stirred for an additional 2 h at 60 °C. The crude product was purified by column chromatography (EtOAc/hexanes, 0:1, 1:19) to give the cycloadduct **5e** (29.6 mg, 0.086 mmol, 90%) as a white solid. R_f = 0.45 (EtOAc/hexanes, 1:9); m.p. 79–80 °C. GC (HP-1 column): retention time 21.650 min. IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 2955 (s), 2871 (w), 1700 (s), 1614 (m), 1492 (m), 1448 (m), 1212 (s), 1189 (s), 1132 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.09 (m, 2 H), 7.41 (m, 3 H), 7.23 (J = 6.9 Hz, d 2 H, 2 H), 7.21 (t, J = 6.9 Hz, 2 H), 7.14 (t, J = 6.9 Hz, 1 H), 4.29 (q, J = 7.1 Hz, 2 H), 3.03 (d, J = 3.7 Hz, 1 H), 3.02 (s, 1 H), 2.92 (d, J = 3.7 Hz, 1 H), 2.71 (br. s, 1 H), 2.67 (br. s, 1 H), 1.63 (dm, J = 9.2 Hz, 2 H), 1.38 (t, J = 7.1 Hz, 3 H), 1.22 (dm, J = 9.2 Hz, 2 H) ppm. ^{13}C NMR (APT, $CDCl_3$, 100 MHz): δ = 163.0, 155.2, 141.0, 132.5, 130.0, 128.9, 128.38, 128.35, 128.0, 127.5, 125.5, 60.1, 47.2, 46.7, 45.2, 37.9, 37.5, 26.42, 26.41, 14.4 ppm. $C_{24}H_{24}O_2$: C 83.69, H 7.02; found C 83.85, H 7.14.

Supporting Information (see also the footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra of all new compounds.

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