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Palladium-catalyzed three-component coupling reaction of organic halides, norbornadiene and terminal alkynes

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Abstract

A three-component coupling reaction of organic halides, including aryl halides, methyl iodine, alkenyl iodine and bromoalkynes, with norbornadiene and terminal alkynes catalyzed by a palladium complex and a phase transfer agent in the presence of aqueous NaOH gave 5,6-disubstituted norbornene derivatives in good yields.

Keywords: Multi-component reaction; Norbornadiene; Bromoalkyne; Terminal alkyne; Dialkynyl norbornene

1. Introduction

Palladium-catalyzed three-component coupling reaction of electrophile and nucleophile into norbornadiene is one of an efficient method to construct *exo-cis*-5,6-disubstituted norbornene derivatives in organic synthesis [1]. In this type of multi-component reaction, various electrophiles including aryl halides (or alkenyl halides) and iodonium salts and diazonium salts with various nucleophiles such as 1-alkynes [2], alkynols [3], organostannanes [4] or tetraphenylborate ion [5] have been used. Interestingly, these types of compounds undergo a retro Diels–Alder reaction at high temperature to give *cis*-olefins. In our previous studies [6], we showed that the reaction of 1-bromo-2-phenylacetylenes with norbornadiene and phenylacetylene in the presence of palladium catalyst and Et_3N afforded unusual multiple-ring formation products, which is constructed from two norbornadiene and two phenylalkynyl groups. In the above reaction Et_3N plays an important role to obtain the corresponding multi-cyclic products. When we changed Et_3N to NaOH and a phase transfer catalyst, we observed entirely different three-component coupling product *exo-cis*-5,6-dialkynyl norbornenes. In this study, we wish to report a palladium-catalyzed three-component coupling reaction of organic halides including alkyl iodine, alkenyl iodine and bromoalkynes with norbornadiene and terminal alkynes in the presence of aqueous NaOH and a phase transfer catalyst to give enynes and endiynes, 5,6-dialkynyl norbornenes, in good yields. Endiynes are versatile organic intermediates in various reactions including cycloaddition reaction [7], metal-catalyzed cyclization reaction [8] and Pauson-Khand reaction [9].

2. Results and discussion

The three-component coupling reaction of iodobenzene **2a** (5.00 mmol), phenylacetylene **3a** (5.00 mmol) and norbornadiene **1** (10.00 mmol) was carried out at 40 °C for 16 h in CH_2Cl_2/1 M aqueous NaOH in the presence of tetrabutylammonium iodide (0.20 mmol) and $Pd(PPh_3)_4$ (0.20 mmol) catalyst to obtain 5,6-disubstituted norbornene derivative **4a** in 81% yield (Scheme 1). The structure of **4a** was characterized by NMR, IR and mass spectroscopic. The *exo* and *cis* stereochemistry of products were conformed by ^1H NMR coupling constant. In the absence of a palladium complex or sodium hydroxide, no product

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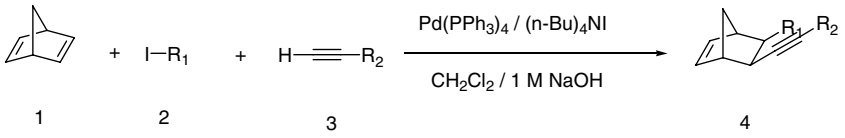


1 2 3 4

2a: R_1 = Ph
2b: R_1 = p-$C_6H_5OCH_3$
2c: R_1 = o-$C_6H_5OCH_3$
2d: R_1 = m-$C_6H_5OCH_3$
2e: R_1 = 2-thiophene
2f : R_1 =3-oxo-cyclohex -1-enyl
2g: R_1 = CH_3

3a: R_2 = Ph
3c: R_2 = CH_2OH
3d: R_2 = $(CH_2)_3CH_3$
3e: R_2 = $Si(CH_3)_3$
3f : R_2 = $C(CH_3)_3$

4a: R_1 = Ph, R_2 = Ph
4b: R_1 = Ph, R_2 = CH_2OH
4c: R_1 = Ph, R_2 = $(CH_2)_3CH_3$
4d: R_1 = Ph, R_2 = H
4e: R_1 = Ph, R_2 = $C(CH_3)_3$
4f : R_1 = p-$C_6H_5OCH_3$, R_2 = Ph
4g: R_1 = o-$C_6H_5OCH_3$, R_2 = Ph
4h: R_1 = m-$C_6H_5OCH_3$, R_2 = Ph
4i : R_1 = 2-thiophene, R_2 = Ph
4 j: R_1 = 2-cyclohexenone, R_2 = Ph
4k: R_1 = CH_3, R_2 = Ph

Scheme 1.

4a was observed, while the omission of phase transfer reagent, tetrabutylammoniun iodide, gave a trace of the desired product **4a**.

Table 1 summarizes the results of the three-component coupling reaction of various organic halides including aryl, alkenyl, methyl halides with norbornadiene and 1-alkynes. Treatment of iodobenzene and norbornadiene with different 1-alkyne **2b**–**2e** (Table 1, entries 1–5) furnished the corresponding 5,6-disubstituted norbornene derivatives **4b**–**4e** in 53–85% yields. In the reaction of iodobenzene and norbornadiene with trimethylsilylacetylene, desilylation product **4d** was obtained (Table 1, entry 4) in 61% yield. It is noteworthy that the reaction shows little steric effect. Therefore, *o*-substituted iodobenzene gave similar yield as that of *m*- and *p*-substituted ones (Table 1, entries 7–9) in 79–83% yields. As shown in entries 6 and 1 (Table 1), the use of bromobenzene instead of iodobenzene in the present reaction required a higher reaction temperature of 90 °C and longer reaction time of 36 h in toluene/1 M NaOH in order to obtain compound **4a** in good yield.

The reaction could further be applied to alkenyl iodides. Under similar reaction conditions, 2-iodothiophene and 3-iodocyclohex-2-enone coupled to norbornadiene **1** and phenylacetylene **3a** to obtain **4i** and **4j** in 82% and 79% yields (Table 1, entries 10–11), respectively. Similarly, methyl iodine reacted with norbornadiene **1** and phenylacetylene **3a** to afford **4k** in 36% yield (Table 1, entries 12). The observed low yield possibly comes form the reaction of methyl iodine with $PPh_3$to give $[PPh_3CH_3]I$.

This ternary coupling was successfully extended to 1-bromoalkyne derivatives and the results are summarized in Table 2. The three-component coupling reaction of 1-bromo-2-phenylacetylene **5a** (5.00 mmol), phenylacetylene **3a** (5.00 mmol) and norbornadiene **1** (10.00 mmol) was carried out at 60 °C for 36 h in toluene/1 M aqueous NaOH in the presence of a catalytic amount of tetrabutylammonium iodide (0.20 mmol) and $Pd(PPh_3)_4$ (0.20 mmol) to provide 5,6-dialkynyl norbornene derivative **6a** in 58% yield (Scheme 2). In addition to **6a**, multiple-ring byproduct **7** was obtained in 18% yield. The results are summarized in Table 2. Compound **6a** was characterized by its NMR, IR and mass spectroscopic data. The *exo* and *cis* stereochemistry was conformed by ^1H NMR coupling constant. Compound **7a** was confirmed by comparing its spectral data with those reported previously [6]. In the absence of a palladium complex or sodium hydroxide, no product **6a** was observed, while the omission of phase transfer reagent, tetrabutylammoniun iodide, gave a trace of the desired product **6a**.

The three-component coupling reaction can be extended to various terminal alkynes **3b**–**3d**. Thus, under similar reaction conditions, 3-methoxyprop-1-yne **3b** and prop-2-yn-1-ol **3c** reacted with norbornadiene **1** and 1-bromo-2-phenylacetylene **5a** to give the corresponding 5,6-dialkynyl norbornene derivatives **6b**–**6c** in 46% and 30% yields, respectively (Table 2, entries 2–3). In the above two reactions, side products **7a** and **6a** were also observed. 1-Bromo-3-methoxypropyne **5b** and propargyl ether **3b** also underwent dialkynylation reaction with **1** to give **6d** in 65% yield (entry 4). No product similar to **7a** was detected in this reaction. Likewise, phenylacetylene **3a** and 1-pentyne **3d**, respectively, reacted with **1** and **5b** to afford the corresponding three-component products **6b** and **6e** in 32% and 33% yields (entries 5 and 6). Again, the side products **6a** and **7a** were found from the reaction of phenylacetylene **3a** with **1** and **5b**. Based on the results shown in Table 2, we concluded that homo-dialkynylation reaction of **1** gave higher yield of the expected product **6** (entries 1 and 4) and less side product was formed.

A proposed mechanism based on the known palladium chemistry for the present palladium-catalyzed dialkynylation of norbornadiene is shown in Scheme 3. Bromoalkyne **2** first undergoes oxidative addition with the phosphine palladium(0) complex to give palladium(II) intermediate (**A**). Exo coordination of norbornadiene to the palladium(II) intermediate and subsequent carbon–carbon double bond insertion leads to a substituted norbornenyl–palladium intermediate (**B**). Substitution of the coordinated bromide by an acetylide to afford a (norbornenyl)(alkynyl)-palladium intermediate (**C**) followed by reductive elimination gives the final 5,6-dialkynyl norbornene product and regenerates the palladium product.

Table 1
Products of 5,6-addition of 1-alkyne **3** and aryl, alkenyl, methyl halides to NBD in the presence of $Pd(PPh_3)_4$

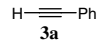
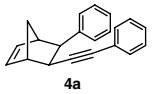
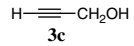
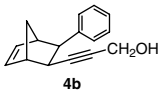
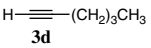
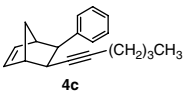
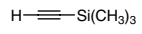
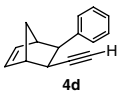
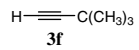
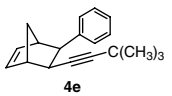
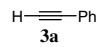
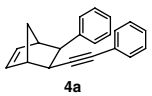
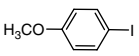
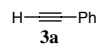
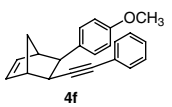
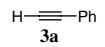
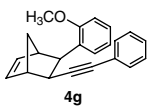
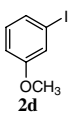
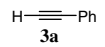
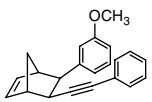
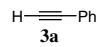
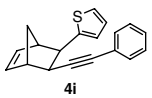
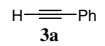
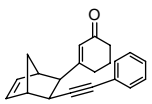
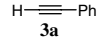
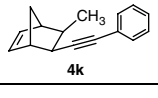
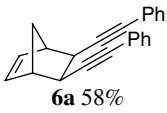
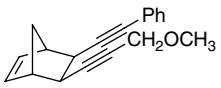
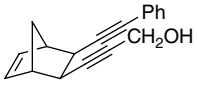
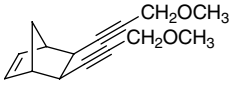
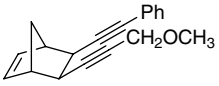
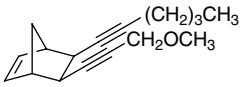
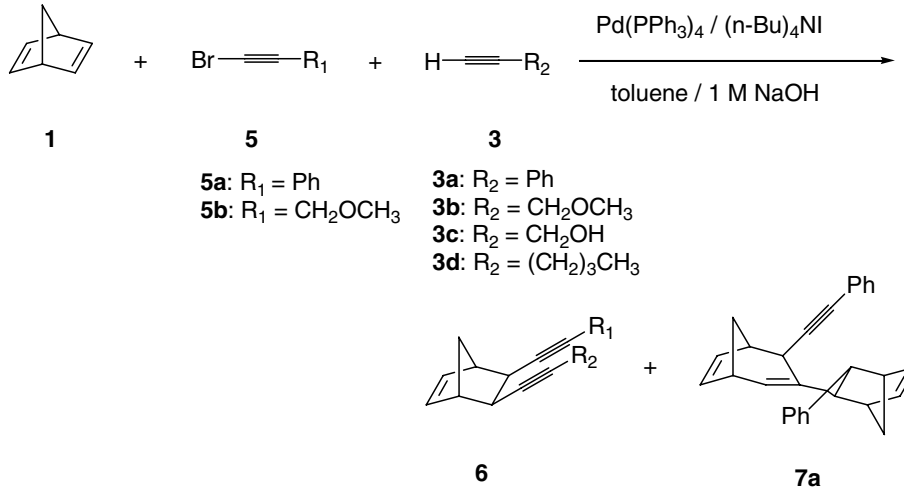
Entry	Organic halides	1-Alkyne	Product yield (%)	
1	 **2a**	 **3a**	 **4a**	81
2	 **2a**	 **3c**	 **4b**	81
3	 **2a**	 **3d**	 **4c**	85
4	 **2a**	 **3e**	 **4d**	61
5	 **2a**	 **3f**	 **4e**	53
6		 **3a**	 **4a**	71
7	 **2b**	 **3a**	 **4f**	79
8	 **2c**	 **3a**	 **4g**	81
9	 **2d**	 **3a**	 **4h**	83
10	 **2e**	 **3a**	 **4i**	82
11	 **2f**	 **3a**	 **4j**	79
12	CH_3I **2g**	 **3a**	 **4k**	36

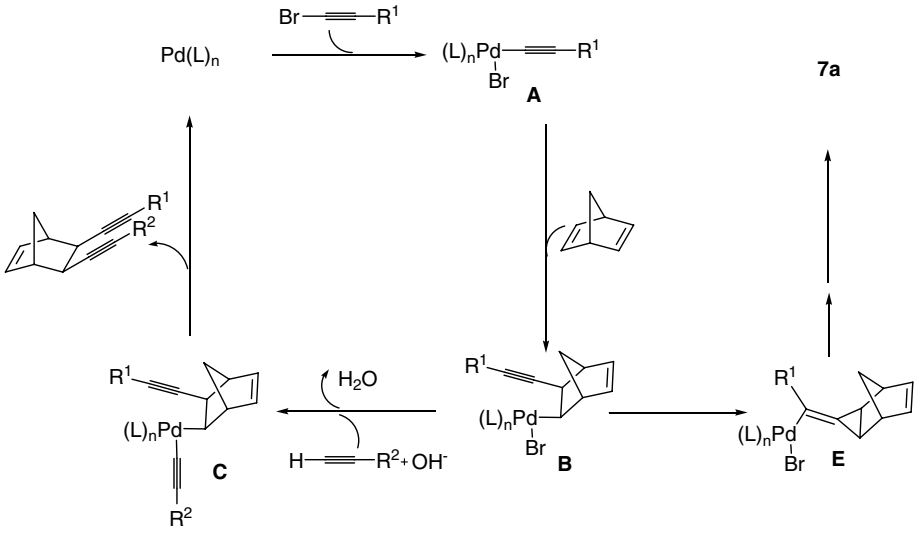
Table 2
Products of 5,6-addition of 1-alkyne **3** and bromoalkyne to NBD in the presence of $Pd(PPh_3)_4$ catalyst

Entry	Bromoalkyne	1-Alkyne	Product yield (%)		
1	Br—≡—Ph **5a**	H—≡—Ph **3a**	 **6a** 58%	**7a** 18	
2	Br—≡—Ph **5a**	H—≡—CH_2OCH_3 **3b**	 **6b** 46%	**7a** 7	**6a** 5
3	Br—≡—Ph **5a**	H—≡—CH_2OH **3c**	 **6c** 30%	**7a** 5	**6a** 13
4	Br—≡—CH_2OCH_3 **5b**	H—≡—CH_2OCH_3 **3b**	 **6d** 65%		
5	Br—≡—CH_2OCH_3 **5b**	H—≡—Ph **3a**	 **6b** 32%	**7a** 4	**6a** 7
6	Br—≡—CH_2OCH_3 **5b**	H—≡—$(CH_2)_3CH_3$ **3d**	 **6e** 33%		



Scheme 2.

The observed results in Table 2 appear to show that the use of aliphatic bromoalkynes and aliphatic terminal alkynes in the present three-component reaction gave the expected dialkynl products **6** without other side products isolated (entries 4 and 6). On the other hand, the use of an aromatic bromoalkyne and/or terminal alkyne led to

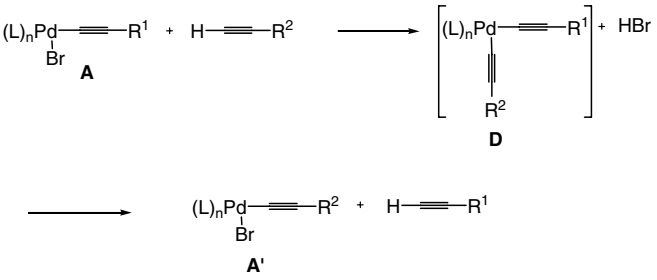


Scheme 3.

the formation of side products **6a** and **7a** (entries 1–3, and 5). This is likely due to the fact that bromoalkynes and terminal alkynes can exchange each other in the transmetallation step.

The observation of side products **6a** and **7a** from the reaction of norbornadiene (**1**) with 1-bromophenylacetylene (**5a**) and terminal alkynes **3b**–**3c** (entries 2 and 3) or from 1-bromoalkynes **5b** and phenylacetylene (entry 5) is intriguing in view of the fact that both 1-bromophenylacetylene (**5a**) and phenylacetylene (**3a**) are required to obtain these two products **6a** and **7a** (entry 1). As a result, it is likely that the exchange of the alkynyl groups between the reagents, 1-bromoalkyne and terminal alkyne, occurred during the palladium-catalyzed reactions (entries 2, 3 and 5) to obtain the side products **6a** and **7a** (*vide infra*). For example, in the reaction of **1** with 1-bromophenylacetylene (**5a**) and methyl propargyl ether (**3b**) (entry 2), we expected that exchange of **5a** with **3b** to give phenylacetylene and methyl 1-bromopropargyl ether (or the equivalent) should occur to some degree. The produced phenylacetylene then reacted with **1** and **5a** under the catalytic conditions to form **6a**.

The mechanism of alkynyl group exchange during the present palladium-catalyzed reaction that likely accounts for the formation of **6a** and **7a** in entries 2, 3 and 5 is not yet clear. A possible pathway for the exchange is shown in Scheme 4. Palladium(II) intermediate (**A**) first undergoes bromide substitution by a new acetylide to give a dialkynyl species (**D**) and HBr. Protonation of the dialkynyl species at the first acetylide ligand affords a new palladium intermediate (**A′**). An evidence for the dialkynyl palladium species **D** is the formation of a trace amount of 1,4-diphenyl-1,3-butadiyne in the reaction of 1-bromophenylacetylene (**5a**) and phenylacetylene (**3a**) with norbornadiene **1**. The 1,3-butadiyne is expected to be from the reductive elimination of **D**. Further evidence for the exchange reaction was obtained from the ^{1}H NMR spectrum of the reaction mixture during the catalytic reactions. One of the alkynyl



Scheme 4.

exchange product phenylacetylene with a characteristic ^{1}H NMR signal at 3.05 ppm for the alkynyl proton can be detected in a small quantity from the reactions in entries 2 and 3 where no phenylacetylene was used at the beginning of the reactions.

The base used in the reaction plays an important role in the competition for the formation of dialkynyl product **6** and multiple-ring product **7a**. Weak base systems such as triethylamine favor the formation of multiple-ring product **7a**, due to the slow addition of the second alkynyl group to the palladium metal center (**B**) via a deprotonation step of the terminal alkyne. As a result, the chance of intramolecular alkyne insertion to give palladium intermediate **E** and finally to multiple-ring product **7a** greatly increases. The employment of strong base NaOH and tetrabutylammonium iodide enhances the rate of addition of the second alkynyl group to **B** and consequently, the formation of the dialkynylation product.

3. Conclusion

5,6-Disubstituted norbornenes were successfully synthesized via a palladium-catalyzed three-component coupling reaction of organic halides, including aryl halides, methyl iodine, alkenyl iodine and bromoalkynes, with norbornadiene and terminal alkynes in the presence of aqueous NaOH

and a phase transfer catalyst. The base used plays an important role in the selectivity of products formed. Further application of the methodology in organic synthesis and detailed mechanistic studies of the catalytic reaction are in progress.

4. Experimental section

4.1. General

All reactions were performed under dry nitrogen atmosphere. ^{1}H and ^{13}C NMR experiments were performed on a Varian Gemini 300 instrument at 300 MHz. Infrared spectra were obtained on a Bomem MB-100 spectrometer. Mass spectra at high resolution were recorded on a JMS-HX110 instrument.

All chemicals were obtained from commercial suppliers and used without further purification unless otherwise noted. The following compounds were prepared according to the published procedures: $Pd(PPh_3)_4$ [10], 1-bromo-2-phenylacetylene [11], methyl 1-bromopropargyl ether [11].

4.2. Experimental procedure

4.2.1. General procedure for the three-component coupling reaction with aryl halide

In a typical procedure, a round-bottom flask containing $Pd(PPh_3)_4$ (0.20 mmol) and $(n\text{-butyl})_4NI$ (0.20 mmol) was purged with nitrogen three times. To the flask were added sequentially norbornadiene (10.00 mmol), iodobenzene (5.00 mmol), 1-alkyne (5.00 mmol), CH_2Cl_2 (5 ml) and NaOH (1 M, 10 ml). The solution was then stirred at 40 °C for 16 h. After filtration through Celite, the filtrate was concentrated and then separated on a silica gel column using a mixture of hexane and ethyl acetate as the eluent.

*4.2.1.1. 5-exo-Phenyl-6-exo-(2-phenylethynyl)bicyclo[2.2.1]-hept-2-ene (**4a**).* ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.71 (dt, $J = 8.7$, $J = 1.8$ Hz, 1H), 2.19 (d, $J = 8.7$ Hz, 1H), 2.97 (dd, $J = 8.9$, $J = 1.8$ Hz, 1H), 3.06 (dd, $J = 8.9$, $J = 1.8$ Hz, 1H), 3.17 (br s, 2H), 6.26 (dd, $J = 4.0$, $J = 2.1$ Hz, 1H), 6.41 (dd, $J = 4.0$, $J = 2.1$ Hz, 1H), 6.86–6.89 (m, 2H), 7.13–7.39 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 37.08 (d), 45.83 (t), 46.15 (d), 48.15 (d), 49.64 (d), 84.23 (s), 92.41 (s), 124.00 (s), 125.92 (d), 127.35 (d), 127.98 (d), 128.02 (d), 128.81 (d), 131.48 (d), 136.77 (d), 140.08 (d), 143.13 (s). IR (neat): 2965, 2218, 1598, 1499, 1451, 911, 749, 695, 668 cm^{-1}. HRMS (*m*/*e*) Calc. for $C_{21}H_{18}$ 270.1409, found 270.1422.

*4.2.1.2. 3-(3-Phenylbicyclo[2.2.1]hept-5-en-2-yl)prop-2-yn-1-ol (**4b**).* ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.66 (dt, $J = 8.8$, $J = 1.7$ Hz, 1H), 2.09 (d, $J = 8.8$ Hz, 1H), 2.74 (dd, $J = 8.9$, $J = 2.0$ Hz, 1H), 2.94 (dd, $J = 8.9$, $J = 2.0$ Hz, 1H), 3.05 (s, 1H), 3.08 (s, 1H), 4.29 (d, $J = 1.2$ Hz, 2H), 6.18 (dd, $J = 5.7$, $J = 3.0$ Hz, 1H), 6.41 (dd, $J = 5.7$, $J = 3.0$ Hz, 1H), 6.86–6.89 (m, 2H), 7.17–7.34 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 36.42 (d), 45.65 (t), 45.94 (d), 48.11 (d), 49.24 (d), 50.92 (t), 82.54 (s), 89.08 (s), 125.97 (d), 127.85 (d), 128.99 (d), 136.67 (d), 140.01 (d), 143.27 (s). IR (neat): 2959, 2144, 1595, 1445, 985 cm^{-1}. HRMS (*m*/*e*) Calc. for $C_{16}H_{16}O$ 224.1201, found 224.1189.

*4.2.1.3. 5-exo-(Hex-1-ynyl)-6-exo-phenylbicyclo[2.2.1]-hept-2-ene (**4c**).* ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.75 (t, $J = 7.2$ Hz, 3H), 1.00–1.05 (m, 4H), 1.63 (dt, $J = 8.7$, $J = 1.7$ Hz, 1H), 1.78–1.84 (m, 2H), 2.10 (d, $J = 8.7$ Hz, 1H), 2.70 (d, $J = 8.8$ Hz, 1H), 2.89 (d, $J = 8.8$ Hz, 1H), 2.98 (s, 1H), 3.05 (s, 1H), 6.16 (dd, $J = 5.4$, $J = 2.8$ Hz, 1H), 6.30 (dd, $J = 5.4$, $J = 2.8$ Hz, 1H), 7.11–7.30 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.57 (q), 18.18 (t), 21.55 (t), 30.7 (t), 36.58 (d), 45.75 (t), 46.30 (d), 47.89 (d), 49.96 (d), 82.08 (s), 83.94 (s), 125.47 (d), 127.47 (d), 127.54 (d), 128.57 (d), 136.56 (d), 139.59 (d), 143.10 (s). IR (neat): 3058, 2946, 2868, 1601, 1453, 1325, 744, 696, 668 cm^{-1}. HRMS (*m*/*e*) Calc. for $C_{19}H_{22}$ 250.1722, found 250.1723.

*4.2.1.4. 5-exo-Ethynyl-6-exo-phenylbicyclo[2.2.1]hept-2-ene (**4d**).* ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.83 (dt, $J = 8.8$, $J = 1.7$ Hz, 1H), 1.93 (d, $J = 2.6$ Hz, 1H), 2.28 (d, $J = 8.8$ Hz, 1H), 2.91 (dd, $J = 8.9$, $J = 1.7$ Hz, 1H), 3.10 (d, $J = 8.9$ Hz, 1H), 3.25 (br s, 1H) 3.24 (br s, 1H), 6.35 (dd, $J = 5.4$, $J = 3.1$ Hz, 1H), 6.52 (dd, $J = 5.4$, $J = 3.1$ Hz, 1H), 7.36–7.50 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 36.20 (d), 45.67 (t), 46.30 (d), 47.70 (d), 49.86 (d), 71.35 (s), 86.37 (s), 126.01 (d), 127.94 (d), 128.75 (d), 136.57 (d), 140.08 (d), 142.61 (s). IR (neat): 3379, 2960, 2210, 1604, 1503, 736, 699 cm^{-1}. HRMS (*m*/*e*) Calc. for $C_{15}H_{14}$ 194.1096, found 194.1082.

*4.2.1.5. 5-exo-(3,3-Dimethylbut-1-ynyl)-6-exo-phenylbicyclo[2.2.1]hept-2-ene (**4e**).* ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.81(s, 9H), 1.61 (dt, $J = 8.6$, $J = 1.8$ Hz, 1H), 2.09 (d, $J = 8.6$ Hz, 1H), 2.66 (d, $J = 8.8$ Hz, 1H), 2.89 (d, $J = 8.9$ Hz, 1H), 2.96 (br s, 1H) 3.05 (br s, 1H), 6.15 (dd, $J = 5.9$, $J = 2.9$ Hz, 1H), 6.32 (dd, $J = 5.9$, $J = 2.9$ Hz, 1H), 7.15–7.30 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 30.58 (q), 36.15 (d), 45.58 (t), 46.11 (d), 47.90 (d), 49.86 (d), 80.56 (s), 92.81 (s), 125.62 (d), 127.76 (d), 128.89 (d), 136.83 (d), 19.82 (d), 143.54 (s). IR (neat): 2958, 2225, 1600, 1490, 1451, 911, 756, 694 cm^{-1}. HRMS (*m*/*e*) Calc. for $C_{19}H_{22}$ 250.1722, found 250.1728.

*4.2.1.6. 5-exo-(4-Methoxyphenyl)-6-exo-(2-phenylethynyl)-bicyclo[2.2.1]hept-2-ene (**4f**).* ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.65 (d, $J = 8.7$ Hz, 1H), 2.15 (d, $J = 8.7$ Hz, 1H), 2.88 (d, $J = 8.8$ Hz, 1H), 2.95 (d, $J = 8.8$ Hz, 1H), 3.05 (br s, 1H), 3.11 (br s, 1H),3.74 (s, 3H), 6.21 (dd, $J = 5.6$, $J = 2.6$ Hz, 1H), 6.39 (dd, $J = 5.6$, $J = 2.6$ Hz, 1H), 6.90–6.97 (m, 4H), 7.13–7.29 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 36.95 (d), 45.62 (t), 46.37 (d), 47.29 (d), 49.47 (d), 55.02 (q), 84.24 (s), 92.56 (s), 113.29 (d), 124.03

(s), 127.22 (d), 127.92 (d), 131.38 (d), 134.95 (d), 136.52 (d), 139.93 (d), 157.98 (s). IR(KBr): 3060, 2980, 2221, 1597, 1444, 1290, 1180, 1028, 751, 694 cm^{-1}. HRMS (*m*/*e*) Calc. for $C_{22}H_{20}O$ 300.1514, found 300.1517.

*4.2.1.7. 5-exo-(2-Methoxyphenyl)-6-exo-(2-phenylethynyl)-bicyclo[2.2.1]hept-2-ene (**4g**).* ^1H NMR (300 MHz, $CDCl_3$): δ 1.63 (d, $J = 8.6$ Hz, 1H), 2.07 (d, $J = 8.6$ Hz, 1H), 2.99 (d, $J = 8.7$ Hz, 1H), 3.12 (s, 1H), 3.18–3.20 (m, 2H), 3.75 (s, 3H), 6.22 (dd, $J = 5.6$, $J = 2.9$ Hz, 1H), 6.35 (dd, $J = 5.6$, $J = 2.9$ Hz, 1H), 6.80–6.84 (m, 2H), 6,97 (t, $J = 7.4$ Hz, 1H), 7.08–7.24 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 36.14 (d), 42.17 (d), 44.37 (d), 45.51 (t), 49.53 (d), 55.27 (q), 82.19 (s), 92.71 (s), 109.83 (d), 120.16 (d), 124.29 (s), 126.50 (d), 126.87 (d), 127.06 (d), 127.92 (d), 131.42 (d), 136.85 (d), 139.52 (d), 158.62 (s). IR (KBr): 2959, 2225, 1595, 1488, 1462, 1291, 1241, 756, 690 cm^{-1}. HRMS (*m*/*e*) Calc. for $C_{22}H_{20}O$ 300.1514, found 300.1519.

*4.2.1.8. 5-exo-(3-Methoxyphenyl)-6-exo-(2-phenylethynyl)-bicyclo[2.2.1]hept-2-ene (**4h**).* ^1H NMR (300 MHz, $CDCl_3$): δ 1.62 (dt, $J = 8.8$, $J = 1.7$ Hz 1H), 2.16 (d, $J = 8.8$ Hz, 1H), 2.94 (dd, $J = 8.9$, $J = 1.7$ Hz, 1H), 2.99 (d, $J = 8.9$ Hz, 1H), 3.13 (br s, 2H), 3.78 (s, 3H), 6.20 (dd, $J = 5.6$, $J = 2.8$ Hz, 1H), 6.38 (dd, $J = 5.6$, $J = 2.8$ Hz, 1H), 6.37–6.80 (m, 5H), 6.88–7.27 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 37.07 (d), 45.86 (t), 46.22 (d), 48.19 (d), 49.61 (d), 55.13 (q), 84.15 (s), 92.34 (s), 111.09 (d), 114.92 (d), 121.45 (d), 124.08 (s), 127.36 (d), 128.04 (d), 131.50 (d), 136.76 (d), 140.03 (d), 144.82 (d), 159.62 (s). IR (neat): 2958, 2224, 1595, 1443, 1318, 1263, 1173, 760, 690 cm^{-1}. HRMS (*m*/*e*) Calc. for $C_{22}H_{20}O$ 300.1514, found 300.1514.

*4.2.1.9. 5-exo-(2-Thiophene)-6-exo-(2-phenylethynyl)bicyclo[2.2.1]hept-2-ene (**4i**).* ^1H NMR (300 MHz, $CDCl_3$): δ 1.70 (d, $J = 8.8$ Hz, 1H), 2.27 (d, $J = 8.8$ Hz, 1H), 2.92 (d, $J = 8.8$ Hz, 1H), 3.12 (s, 1H), 3.17 (s, 1H), 3.27 (d, $J = 8.8$ Hz, 1H), 6.23 (dd, $J = 5.5$, $J = 2.9$ Hz, 1H), 6.36 (dd, $J = 5.6$, $J = 2.9$ Hz, 1H), 6.89 (d, $J = 2.7$ Hz, 1H), 6.98 (dd, $J = 5.2$, $J = 2.7$ Hz, 1H), 7.09 (d, $J = 5.2$ Hz, 1H), 7.12–7.24 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 37.41 (d), 44.07 (d), 45.79 (d), 48.93 (t), 49.95 (d), 84.09 (s), 91.63 (s), 123.44 (d), 124.06 (s), 125.00 (d), 126.30 (d), 127.48 (d), 128.12 (d), 131.60 (d), 136.86 (d), 139.28 (d), 146.86 (s). IR (neat): 3109, 2190, 1595, 1486, 1442, 1213, 753, 688 cm^{-1}. HRMS (*m*/*e*) Calc. for $C_{19}H_{16}S$ 276.0973, found 276.0960.

*4.2.1.10. 5-exo-(3-Oxo-cyclohex-1-enyl)-6-exo-(2-phenylethynyl)bicyclo[2.2.1]hept-2-ene (**4j**).* ^1H NMR (300 MHz, $CDCl_3$): δ 1.62 (d, $J = 8.9$ Hz, 1H), 1.96–2.01 (m, 3H), 2.23–2.42 (m, 4H), 2.60 (dt, $J = 15$, $J = 4.8$ Hz, 1H), 2.95 (d, $J = 8.8$ Hz, 1H), 3.00 (s, 1H), 3.12 (s, 1H), 6.05 (s, 1H), 6.22 (dd, $J = 5.5$ Hz, $J = 2.9$ Hz, 1H), 6.30 (dd, $J = 5.5$ Hz, $J = 2.9$ Hz, 1H), 7.20–7.28 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.24 (t), 31.65 (t), 35.50 (d), 37.37 (t), 44.30 (d), 45.27 (t), 50.08 (d), 50.19 (d), 82.68 (s), 90.97 (s), 123.55 (s), 124.92 (d), 127.92 (d), 128.44 (d), 131.49 (d), 136.94 (d), 139.29 (d), 168.41 (s), 200.46 (s). IR (KBr): 2929, 2224, 1661, 1627, 1436, 1250, 1189, 755, 695 cm^{-1}. HRMS (*m*/*e*) Calc. for $C_{21}H_{20}O$ 288.1514, found 288.1510.

*4.2.1.11. 5-exo-Methyl-6-(2-phenylethynyl)bicyclo[2.2.1]-hept-2-ene (**4k**).* ^1H NMR (300 MHz, $CDCl_3$): δ 1.24 (d, $J = 7.3$ Hz, 3H), 1.42 (dt, $J = 8.9$, $J = 1.8$ Hz, 1H), 1.74–1.81 (m, 2H), 2.51–2.56 (m, 2H), 2.99 (s, 1H), 6.10 (dd, $J = 5.7$, $J = 2.9$ Hz, 1H), 6.23 (dd, $J = 5.7$, $J = 2.9$ Hz, 1H), 7.28–7.34 (m, 3H), 7.28–7.34 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.60 (q), 34.94 (d), 35.66 (d), 43.60 (t), 48.66 (d), 50.08 (d), 82.46 (s), 92.58 (s), 124.50 (s), 127.51 (d), 128.32 (d), 131.69 (d), 135.61 (d), 138.87 (d). IR (neat): 2958, 2197, 1598, 1489, 1447, 1266, 756, 691 cm^{-1}. HRMS (*m*/*e*) Calc. for $C_{16}H_{16}$ 208.1252, found 208.1253.

4.2.2. General procedure for the three-component coupling reaction with bromoalkyne

In a typical procedure, a round-bottom flask containing $Pd(PPh_3)_4$ (0.20 mmol) and $(n\text{-butyl})_4NI$ (0.20 mmol) was purged with nitrogen three times. To the flask were added sequentially norbornadiene (10.00 mmol), bromoalkyne (5.00 mmol), 1-alkyne (5.00 mmol), toluene (30 ml) and NaOH (1 M, 10 ml). The solution was then stirred at 60 °C for 36 h. After filtration through Celite, the filtrate was concentrated and then separated on a silica gel column using a mixture of hexane and ethyl acetate as the eluent.

*4.2.2.1. 5-exo-6-exo-Bis(2-phenylethynyl)bicyclo[2.2.1]-hept-2-ene (**6a**).* ^1H NMR ($CDCl_3$, 300 MHz): δ 1.60 (dt, $J = 8.9$, $J = 1.7$ Hz, 1H), 2.10 (d, $J = 8.9$ Hz, 1H), 2.78 (d, $J = 1.7$ Hz, 2H), 3.12 (br s, 2H), 6.20 (br s, 2H), 7.20–7.26 (m, 6H), 7.37–7.40 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 36.19 (d), 45.67 (t), 49.75 (t), 83.67 (s), 91.63 (s), 124.22 (s), 127.67 (s), 128.25 (d), 131.90 (d), 137.32 (d). IR (neat): 3058, 2979, 2225, 1598, 1489,1324, 911, 755, 689 cm^{-1}. HRMS (*m*/*e*) Calc. for $C_{23}H_{18}$ 294.1409, found 294.1406.

*4.2.2.2. 5-exo-(3-Methoxyprop-1-ynyl)-6-exo-(2-phenylethynyl)bicyclo[2.2.1]hept-2-ene (**6b**).* ^1H NMR ($CDCl_3$, 300 MHz): δ 1.56 (dt, $J = 9.0$, $J = 1.7$ Hz, 1H), 2.01 (d, $J = 9.0$ Hz, 1H), 2.59 (dd, $J = 8.4$, $J = 1.7$ Hz, 1H), 2.69 (dd, $J = 8.4$, $J = 1.7$ Hz, 1H), 3.02 (br s, 1H), 3.07 (br s, 1H), 3.31 (s, 3H), 4.15 (d, $J = 1.9$ Hz, 2H), 6.15 (br s, 2H), 7.25–7.30 (m, 3H), 7.43–7.46 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 35.49 (d), 35.67 (d), 45.46 (t), 49.53 (d), 49.6 (d), 57.02 (q), 60.06 (t), 78.67 (s), 83.45 (s), 88.12 (s), 91.39 (s), 124.16 (s), 127.62 (s), 128.20 (d), 131.66 (d), 136.67 (d), 137.10 (d) ppm. IR (neat): 2965,

2232, 1490, 1244, 849, 726 cm^{-1}. HRMS (*m*/*e*) Calc. for $C_{19}H_{18}O$ 262.1358, found 262.1370.

*4.2.2.3. 5-exo-(2-Phenylethynyl)-6-exo-(3-hydroxyprop-1-ynyl)bicyclo[2.2.1]hept-2-ene (**6c**).* ^1H NMR ($CDCl_3$, 300 MHz): δ 1.55 (dt, $J = 8.9$, $J = 1.8$ Hz, 1H), 1.99 (d, $J = 8.9$ Hz, 1H), 2.58 (dd, $J = 8.4$, $J = 1.8$ Hz, 1H), 2.69 (dd, $J = 8.4$, $J = 1.8$ Hz, 1H), 3.01 (br s, 1H), 3.08 (br s, 1H), 4.30 (d, $J = 2.0$ Hz, 2H), 6.15 (br s, 2H), 7.27–7.35 (m, 3H), 7.43–7.46 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 35.49 (d), 35.77 (d), 45.47 (t), 49.40 (d), 49.59 (d), 51.32 (t), 81.47 (s), 83.57 (s), 87.65 (s), 91.52 (s), 124.06 (s), 127.84 (s), 128.43 (d), 131.63 (d), 136.74 (d), 137.10 (d). IR (neat): 2962, 2222, 1558, 1260, 1093, 758, 693 cm^{-1}. HRMS (*m*/*e*) Calc. for $C_{18}H_{16}O$ 248.1201, found 248.1189.

*4.2.2.4. 5-exo-6-exo-Bis(3-methoxyprop-1-ynyl)bicyclo[2.2.1]-hept-2-ene (**6d**).* ^1H NMR ($CDCl_3$, 300 MHz): δ 1.51 (dt, $J = 8.9$, $J = 1.8$ Hz, 1H), 1.91 (d, $J = 8.9$ Hz, 1H), 2.51 (d, $J = 1.8$ Hz, 2H), 2.98 (br s 2H), 3.39 (s, 6H), 4.14 (s, 4H), 6.13 (br s, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 34.93 (d), 45.15 (t), 49.31 (d), 56.73 (q), 59.78 (t), 78.43 (s), 87.86 (s), 136.83 (d). IR (neat): 2935, 2226, 1653, 1451, 1094, 905, 698 cm^{-1}. HRMS (*m*/*e*) Calc. for $C_{15}H_{18}O_2$ 230.1307, found 230.1313.

*4.2.2.5. 5-exo-(Hex-1-ynyl)-6-exo-(3-methoxyprop-1-ynyl)-bicyclo[2.2.1]hept-2-ene (**6e**).* ^1H NMR ($CDCl_3$, 300 MHz): δ 0.93 (t, $J = 7.0$ Hz, 3 H), 1.41–1.53 (m, 5H), 1.92 (d, $J = 8.8$ Hz, 1H), 2.23 (td, $J = 6.8$, $J = 1.9$ Hz, 2H), 2.47–2.49 (m, 2H), 2.93 (br s, 1H), 2.97 (br s, 1H), 3.42 (s, 3H), 4.17 (d, $J = 1.8$ Hz, 2H), 6.11 (br s, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.39 (q), 18.36 (t), 21.67 (t), 31.07 (t), 35.15 (d), 35.21 (d), 45.35 (t), 49.60 (d), 49.86 (d), 57.03 (d), 60.15 (t), 78.29 (s), 81.24 (s), 83.18 (s), 88.64 (s), 136.92 (d), 137.25 (d) ppm. IR (neat): 2935, 2220, 1655, 1448, 1090, 756, 691 cm^{-1}. HRMS (*m*/*e*) Calc. for $C_{17}H_{22}O$ 242.1671, found 242.1675.

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