Effects of Substituents on the Multiple Bonds on Ring-Closing Metathesis of Enynes

Tsuyoshi Kitamura, Yoshihiro Sato, Miwako Mori*

Graduate School of Pharmaceutical Sciences, Hokkaido University, Sapporo 060-0812, Japan
Fax: (+81)-11-706-4982, e-mail:mori@pharm.hokudai.ac.jp

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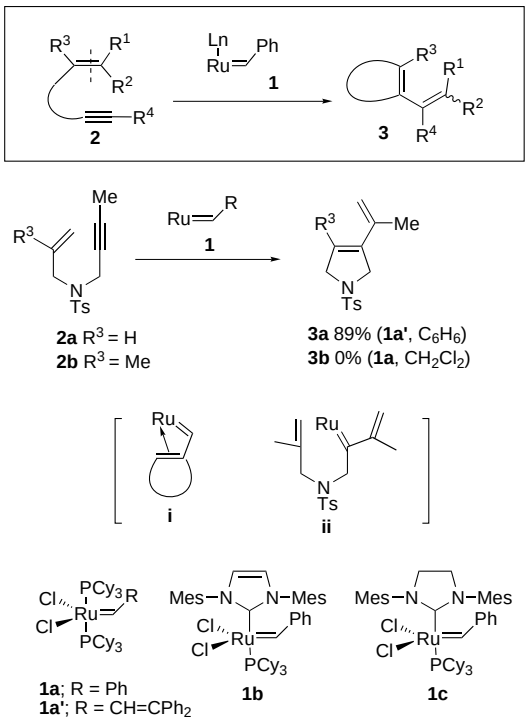
Abstract: In ring-closing metathesis (RCM) reactions of enynes, the substituents on the multiple bonds are quite important. Although RCM of an enyne having a monosubstituted alkene proceeds smoothly using the first-generation ruthenium-carbene complex **1a**, that of an enyne having a disubstituted alkene and internal alkyne using **1a** does not proceed. However, the second-generation ruthenium-carbene complex **1b** or **1c** containing an *N*-heterocyclic carbene as a ligand was found to be very effective for such an enyne, and the two-metathesis products were formed in high yields.

Keywords: 1,3-diene; enyne; homogeneous catalysis; metathesis, ring-closing metathesis (RCM); ruthenium

Introduction

Transition metals have played important roles in recent synthetic organic chemistry, and they are essential tools for the total syntheses of natural products. A metathesis reaction[1] using a metal-carbene complex is quite interesting because multiple bonds, such as double bonds and even triple bonds, are cleaved and, at the same time, multiple bonds are formed. Ring-closing metathesis (RCM) of enynes[2,3] is a very attractive reaction, because a carbon-carbon double bond is formed between the alkene carbon and the alkyne carbon, while the double bond of the enyne is cleaved and the alkylidene part of alkene migrates to the alkyne carbon to give a cyclized compound having a diene moiety. In this reaction, the substituents on the alkyne part or the alkene part are important. It has been shown that the reaction rate of RCM of enyne having a terminal alkyne using ruthenium-carbene complex **1a** is slow because the diene moiety of the product reacts with the methylideneruthenium-carbene complex to form ruthenium-carbene complex **i**.[2a] However, in this case, the reaction proceeded smoothly under ethylene gas.[2d] On the other hand, the effect of the substituent on the alkene is also important. RCM of enyne **2a** ($R^3 = H$) having a monosubstituted alkene and an internal alkyne using **1a** proceeded smoothly, and the cyclized product **3a** was obtained in high yield.[2a] However, when enyne **2b** ($R^3 = Me$) having a 1,1-disubstituted alkene was treated with **1a** in a similar manner, no cyclized product **3b** was formed and the starting material **2b** was recovered. This means that the ruthenium-carbene complex **ii** formed by the reaction of the alkyne part of enyne **2b** and **1a** cannot react with the 1,1-disubstituted alkene.

Recently, the new generation of ruthenium-carbene complex **1b** or **1c** containing an *N*-heterocyclic carbene as a ligand has been reported.[4] It was shown that the reactivities of these complexes are higher than that of **1a** in olefin metathesis and that RCM of dienes having a 1,1-disubstituted alkene proceeded smoothly using **1b**[4b–e] or **1c**[4f] to give a cyclized product having a tri-



Scheme 1. Ruthenium-catalyzed intramolecular enyne metathesis.

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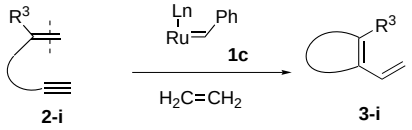
or tetrasubstituted olefin. Thus, we tried to use the second-generation ruthenium-carbene complex **1b** or **1c** for enyne metathesis, and examined the effects of the substituents on the multiple bonds.[2j]

Results and Discussion

RCM of an Enyne Having a 1,1-Disubstitued Olefin and a Terminal Alkyne

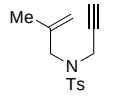
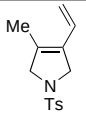
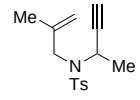
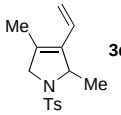
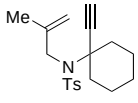
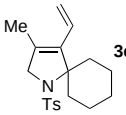
At first, we tried the RCM of enyne **2a** using **1b** as a catalyst. When a toluene solution of **2a** and 1 mol % of **1b** was stirred at 80° C for 1 h, the desired cyclized compound **3a** was obtained in 71% yield, indicating that second-generation ruthenium catalyst **1b** can be used in RCM of enynes. Subsequently, the RCM of enynes **2 – i** having a 1,1-disubstituted alkene and a terminal alkyne were carried out under ethylene gas (Scheme 2). A toluene solution of **2c** and 5 mol % of **1c** was stirred at 80° C under an atmosphere of ethylene. After only 15 min, the spot of the starting material disappeared on TLC and the desired product **3c** was obtained in 30% yield after the usual work-up (Table 1, run 1).

The enynes **2d** and **2e** having allyl group substituents at a propargylic position gave **3d** and **3e** in 83% and 89% yields, respectively (Runs 2 and 3). Presumably, the large substituents on the five-membered ring inhibited further reaction of the diene moiety of the products with the second-generation ruthenium-carbene complex **1c** due to steric hindrance, thus, resulting in the higher yields of **3d** and **3e** compared with that of **3c**.



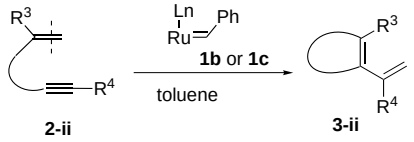
Scheme 2. Reactions of enynes having a 1,1-disubstituted alkene and a terminal alkyne.

Table 1. Reaction of enynes having a 1,1-disubstituted alkene and a terminal alkyne using **1c**.

Run	Substrate		Conditions	Product		Yield [%]
1		**2c**	80 °C, 15 min		**3c**	30%
2		**2d**	60 °C, 1 h		**3d**	83%
3		**2e**	80 °C, 3 h		**3e**	89%

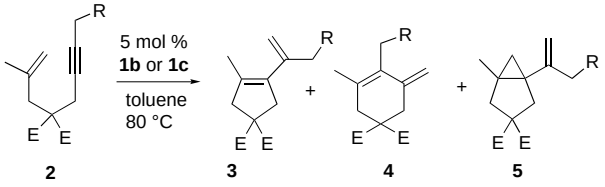
RCM of an Enyne Having a 1,1-Disubstituted Alkene and an Internal Alkyne

Subsequently, RCM of enyne **2-ii** having a 1,1-disubstituted alkene and an internal alkyne using a second-generation ruthenium-carbene complex was examined.



Scheme 3. RCM of an enyne having a 1,1-disubstituted alkene and an internal alkyne using **1b** or **1c**.

When a toluene solution of enyne **2f** and 5 mol % of **1b** was warmed at 80° C for 5 h, two metathesis products, **3f** and **4f**, were obtained in 85% yield along with compound **5f** having a three-membered ring in 5% yield. The former compounds, **3f** and **4f**, were obtained as a mixture of two inseparable isomers, but they could be isolated by repeated chromatography on silica gel. Compound **3f** has a five-membered ring, which was usually formed by the reaction of an enyne having a monosubstituted alkene and **1a**.[2] This would be produced by carbon-carbon bond formation between the disubstituted alkene carbon (C7) and the inside carbon (C3) of the alkyne, while the methylene carbon of the disubstituted alkene migrated to the outside carbon (C2) of the alkyne. On the other hand, the ^{1}H NMR spectrum of compound **4f** is similar to that of **3f**, and other spectral data such ^{13}C NMR, HMQC, HMBC, and mass spectra agreed with this structure. This should be produced by carbon-carbon bond formation between the disubstituted alkene carbon (C7) and the outside alkyne carbon (C2), while the methylene carbon of the alkene migrated to the inside alkyne carbon (C3).

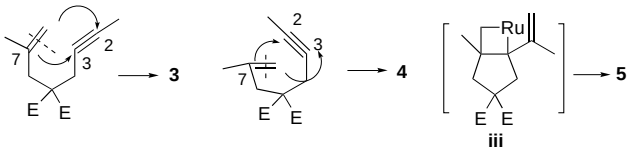


Scheme 4. Reaction of **2** with ruthenium catalyst **1**.

Compound **5f** would be formed by reductive elimination from ruthenacyclobutane **iii** as shown in Scheme 5. When ruthenium-carbene complex **1c** was used for this reaction, the same compounds **3f** and **4f** were obtained in 42% and 41% yields, respectively, along with a small amount of **5f** (Table 2, run 2).[5] This indicates that the six-membered ring compound **4f** was formed when the 1,6-enyne was treated with the second-generation ruthenium carbene complex **1b** or **1c**.[6] Furthermore, enyne **2g** having an acetoxymethyl group on the alkene part was examined, but **3g** was obtained in

Table 2. Reaction of an enyne with the second-generation ruthenium-carbene complex **1b**.

Run	R	E		Ru	Time [h]	Yield [%] of 3	4	5	2
1	H	CO_2Et	**2f**	**1b**	5	43	42	5	-
2	H	CO_2Et	**2f**	**1c**	5	42	41	3	-
3	OAc	CO_2Me	**2g**	**1c**	24	12	-	-	71
4	OH	CO_2Me	**2h**	**1c**	2	45	34	-	-

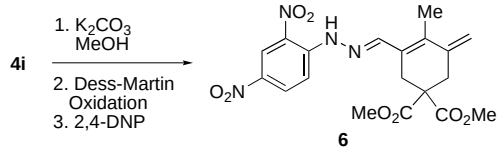


Scheme 5. Formal reaction course.

only 12% yield. On the other hand, enyne **2h** gave **3h** and **4h** in 45% and 34% yields, respectively. Presumably, the steric effect of the acetoxy group on the alkyne part resulted in the low yield of the cyclized product **3g**.

Various enynes were treated with **1b** in a similar manner, and the results are shown in Table 3. The enyne metathesis products **3** and **4** were obtained as an inseparable mixture of two isomers. Thus, the their ratios were determined by ^{1}H NMR spectroscopy.[7] In each case, a small amount of **5** was obtained.

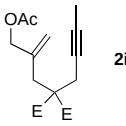
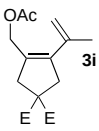
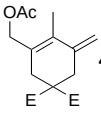
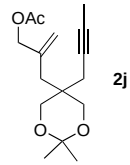
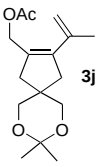
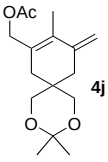
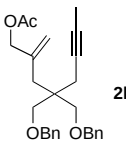
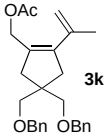
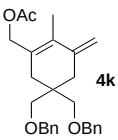
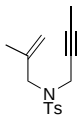
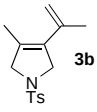
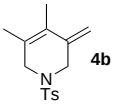
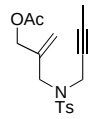
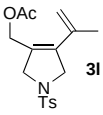
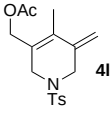
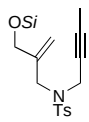
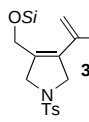
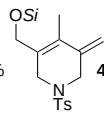
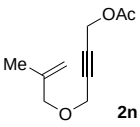
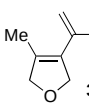
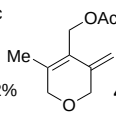
Although the structure of compound **4** was demonstrated by the spectral data, it was further confirmed by X-ray crystallographic analysis. Treatment of compound **4i** with K_2CO_3 in MeOH followed by Dess–Martin oxidation[8] afforded the aldehyde, which was converted into the 2,4-dinitrophenylhydrazone **6** (Scheme 6). The X-ray crystallographic structure[9] of **6** is shown in Figure 1. Apparently, a six-membered ring is formed in this reaction.



Scheme 6. Conversion of **4i** into its 2,4-dinitrophenylhydrazone **6**.

The reaction of enyne **2o** having a 1,1-disubstituted alkene and a terminal alkyne with a methyl group at a propargylic position with **1c** was carried out in a similar manner to give **3o** and **4o** in 68% and 30% yields, respectively. However, enyne **2p**, which has large substituents close to the alkyne part, did not afford the metathesis product due to steric hindrance.

Table 3. Reaction of **1b** with enynes having a 1,1-disubstituted alkene and an internal alkyne.[a]

Run	Substrate	Conditions	Products, yield[b]		
1		**2i** 80 °C 5 h	 **3i** 50%	 **4i** 39%	
2		**2j** 80 °C 6 h	 **3j** 47%	 **4j** 27%	
3		**2k** 80 °C 24 h	 **3k** 50%	 **4k** 42%	
4		**2b** 80 °C 6 h	 **3b** 34%	 **4b** 30%	
5		**2l** 50 °C 3 h	 **3l** 41%	 **4l** 30%	
6		**2m**[c] 50 °C 24 h *Si* = TBDMS	 **3m** 29%	 **4m** 17%	
7		**2n** 80 °C[d] 1 h	 **3n** 22%	 **4n** 69%	

[a] All reactions were carried out using **1b** (5 mol %) in toluene.
[b] All yields were calculated from ^{1}H NMR spectra after isolation as a mixture of two isomers.
[c] 10 mol % of **1b** was used.
[d] 2.5 mol % of **1b** was used.

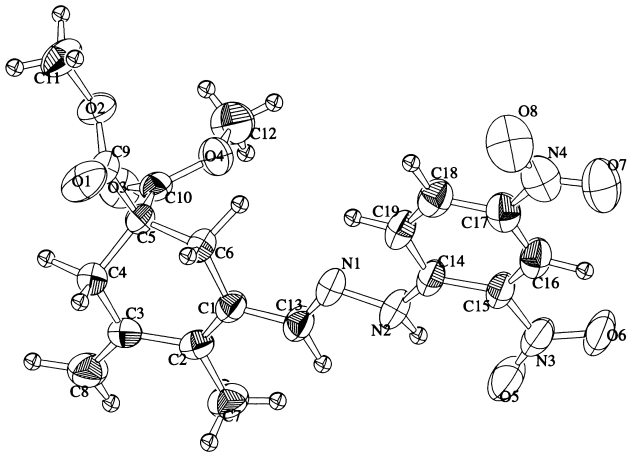
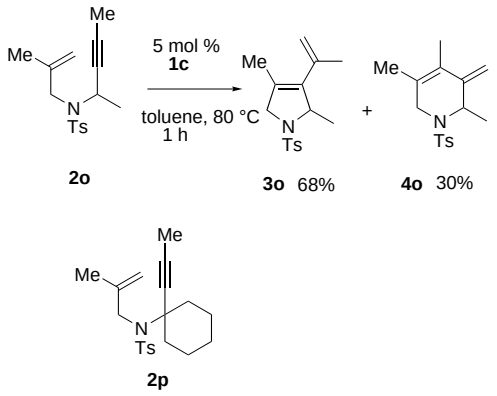


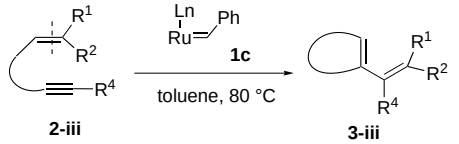
Figure 1. X-ray crystallographic analysis of **6**.



Scheme 7. Reaction of **2o** with **1c**.

RCM of an Enyne Having a Di- and Trisubstituted Alkene and an Internal Alkyne

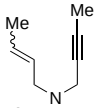
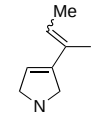
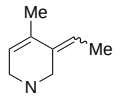
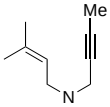
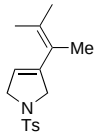
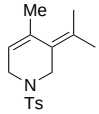
Subsequently, the RCM of enyne **2-iii** having a di- and trisubstituted alkene and an internal alkyne with **1c** was carried out. The RCM of enyne **2q** having a 1,2-disubstituted alkene and an internal alkyne using **1a** did not proceed.



Scheme 8. Reaction of an enyne having a substituted alkene and an internal alkyne with **1c**.

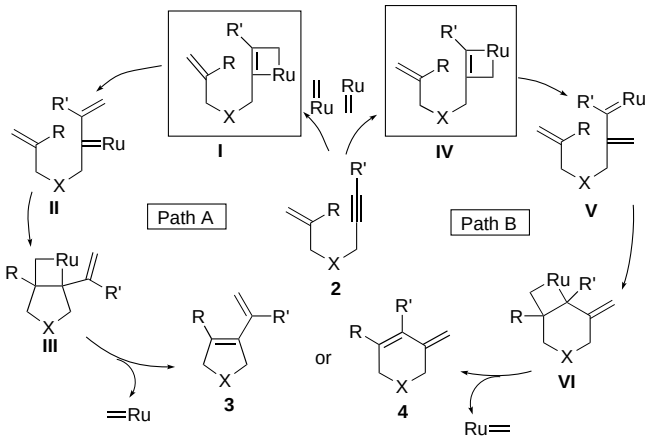
When enyne **2q** was treated with **1c** in a similar manner, the metathesis products **3q** and **4q** were obtained in high yields. Surprisingly, the trisubstituted alkene **2r** was also cleaved, and the five- and six-membered ring compounds **3r** and **4r** were obtained in 56% and 32% yields, respectively.

Table 4. RCM of enynes having a substituted alkene and an internal alkyne using **1c**.

Run	Substrate	Time	Product [%]	
1	 **2q** (*E*/*Z* = 3.4/1)	45 min	 **3q** 50%(*E*/*Z* = 1/1)	 **4q** 32%(*E*/*Z* = 1.31)
2	 **2r**	30 min	 **3r** 56%	 **4r** 32%

Possible Reaction Courses

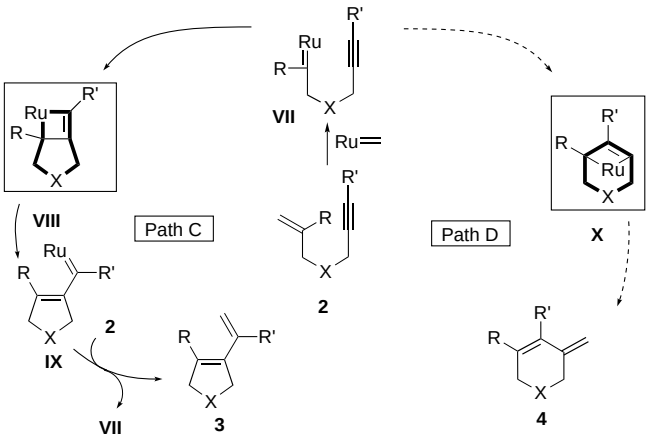
The possible reaction course is shown in Scheme 9. If RCM proceeds by reaction of the alkyne part of the



Scheme 9. Two possible reaction pathways for enyne metathesis – the ruthenium-carbene complex reacts first with the alkyne part.

enyne with the methylideneruthenium-carbene complex, two reaction pathways are possible. That is, if ruthenium metal combines with the inside carbon of the alkyne (path A), the ruthenacyclobutene **I** would be formed. Then, ring opening of **I** would produce ruthenium-carbene complex **II** and intramolecular [2 + 2] cycloaddition would occur to give **III**. Thus, the smaller-ring-sized product **3** is formed (five-membered ring). However, when the ruthenium metal of a carbene complex combines with the outside carbon of the alkyne, ruthenacyclobutene **IV** would be formed, and it would be converted into ruthenium-carbene complex **V** by ring opening. This would then react with the alkene part intramolecularly by [2 + 2] cycloaddition to give ruthenacyclobutane **VI**, which would afford the six-membered ring compound **4** (path B).[6]

As another possible reaction course, if carbene complex first reacts with the alkene part, the ruthenium-carbene complex **VII** would be formed. When **VII** reacts with the alkyne part, two reaction pathways should be considered. One is the formation of ruthenacyclobutene **VIII** fused by the five-membered ring (path C). The ring opening of **VIII** would afford ruthenium carbene complex **IX** and it would react with the alkene part of the starting material **2** to give the five-membered ring compound **3** and the ruthenium-carbene complex **VII** would be formed. The other is the formation of **X** from **VII** by combining the ruthenium metal with the inside carbon of the alkyne (path D). However, ruthenacyclobutene **X** has a highly strained structure. Thus, the reaction did not proceed in this way (path D). Although the reaction of ruthenium-carbene



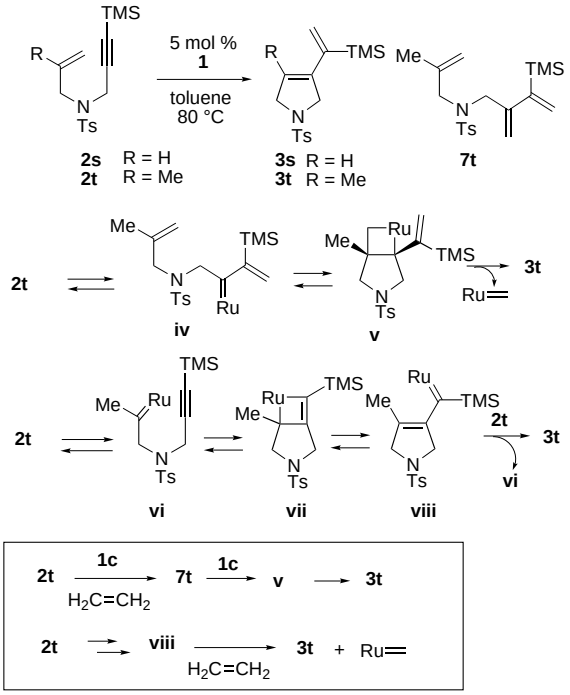
Scheme 10. Two possible reaction pathways of enyne metathesis - the ruthenium-carbene complex reacts first with the alkene part.

complex **1b** or **1c** with the alkyne part gives five- and six-membered ring compounds via path A and path B, if ruthenium carbene complex **1b** or **1c** reacts with the alkene part, only a five-membered ring compound would be formed.

Although the reason why RCM of enyne **2** having a monosubstituted alkene or a terminal alkyne gave only **3**, while that of enyne **2** having a disubstituted alkene and an internal alkyne with the second-generation ruthenium carbene complex **1b** or **1c** gave **3** and **4** is not clear, the results are quite interesting.

RCM of an Enyne Having a TMS Group on the Alkyne

The effect of a TMS group on the alkyne part was examined. We have already reported that a TMS group on the alkyne affected the reaction rate of RCM. That is, a benzene solution of **2s** was stirred in the presence of the first-generation ruthenium-carbene complex **1a** to afford **3s** in low yield.[2a] When 5 mol % of **1b** was used in RCM of **2t**, the five-membered ring compound **3t** was obtained in 28% yield (Table 5, run 1). The use of **1c** as a catalyst slightly increased the yield of **3t** (run 3). In this reaction, a six-membered ring compound was not formed. If the ruthenium-carbene complex reacts with the alkyne part of **2t** first to form ruthenium-carbene complex **iv** which then reacts with the alkene part intramolecularly, ruthenacyclobutane **v** would be formed and it would be converted into **3t** and a methylidenecarbene complex. However, if the ruthenium-carbene complex reacts with the alkene part of **2t** first, ruthenium-carbene complex **vi** would be formed and then it would react intramolecularly with the alkyne part to give ruthenium-carbene complex **viii** *via* **vii**. Then it would react with the alkene part of **2t** to afford **3t**, and **vi** would be regenerated. If this reaction is carried



Scheme 11. RCM of an enyne having a TMS group on the alkyne part.

out under ethylene gas, **7t** would be produced by cross-enyne metathesis of the alkyne part of **2t** and ethylene, and intramolecular olefin metathesis should give **3t** via **v**. On the other hand, the reaction of ruthenium-carbene complex **viii** and ethylene, not **2t**, should give easily **3t**. This means that the reaction rate should be accelerated under ethylene gas.

Thus, when the reaction was carried out using **1b** under an atmosphere of ethylene, the yield of **3t** increased to 40% (run 2) along with **7t** in 18% yield, and the use of **1c** under ethylene gas gave **3t** in 64% yield along with **7t** in 6% yield (run 4). When 10 mol % of **1c** was used for this reaction, the yield of **3t** increased to 84% (run 5).

Table 5. Reaction of enyne **2t** having a 1,1-disubstituted alkene and an alkyne having a TMS group.

			Yield [%] of		
Run	Ru [mol %]	Gas	**3t**	**7t**	**2t**
1	**1b** (5)	Ar	28	0	59
2	**1b** (5)	ethylene	40	18	40
3	**1c** (5)	Ar	33	0	57
4	**1c** (5)	ethylene	64	6	26
5	**1c** (10)	ethylene	84	11	—

These results indicated that in the enyne metathesis of **2t** using **1b** or **1c**, the reaction rate was accelerated by ethylene gas. Since the cyclized compound **3t** has a TMS group on the diene moiety, it would be a useful precursor in synthetic organic chemistry.

Conclusion

RCM of enynes having a monosubstituted alkene or a terminal alkyne proceeded smoothly using first- and second-generation ruthenium-carbene complexes to give smaller-ring-sized compounds. The second-generation ruthenium carbene complex **1b** or **1c** was very effective for RCM of an enyne having substituents on the alkene part and the alkyne part, although the use of first-generation ruthenium carbene complex **1a** was not effective for RCM of these enynes. In these RCM of enynes, two metathesis products were formed. Presumably, the steric effect on the multiple bond affected the ring size of the products and their ratio.

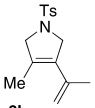
Experimental Section

General Information

The metathesis reactions were carried out under an atmosphere of argon or ethylene, and the reaction solutions were degassed through freeze-pump-thaw cycle. All solvents and reagents were purified when necessary using standard procedures. Ethylene gas was purified by passage through the aqueous CuCl solution (2 g of CuCl in 180 mL of saturated aqueous NH_4Cl) and concentrated H_2SO_4 and then a KOH tube. Catalysts **1a** and **1c** were purchased from Strem Chemicals, and catalyst **1b** was prepared according to the literature procedure.[4e]

Typical Procedure for the Metathesis Reaction of 2i

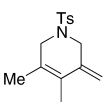
To a solution of **2i** (34.2 mg, 115 μmol) in toluene (3.8 mL, 0.03 M) was added **1b** (4.9 mg, 5.8 μmol, 5 mol %), and the solution was warmed at 80°C for 5 h under an argon atmosphere. After the solvent was removed, the residue was purified by flash column chromatography on silica gel (hexane/benzene/ethyl acetate, 8:1:2) to afford **3i** (17.1 mg, 58 μmol, 50%), and **4i** (13.3 mg, 46 μmol, 39%) as a colorless oil, respectively.



3b

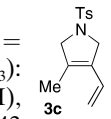
3-Isopropenyl-4-methyl-1-(4-toluenesulfonyl)-2,5-dihydro-1*H*-pyrrole (3b): IR (film): ν = 1646, 1598, 1344, 1163 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.75 (s, 3H), 1.87 (s, 3H), 2.43 (s, 3H), 4.07 (br, 2H), 4.19 (m, 2H), 4.74 (s, 1H), 4.96 (s, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 13.0 (CH_3), 21.5 (CH_3), 22.4 (CH_3), 57.0 (CH_2), 60.1 (CH_2), 115.4 (CH_2), 127.5 (CH × 2), 129.0 (C), 129.7 (CH × 2), 131.0 (C), 134.1 (C), 137.7 (C), 143.4 (C).

4,5-Dimethyl-3-methylene-1-(4-toluenesulfonyl)-1,2,3,6-tetrahydropyridine (4b): IR (film): ν = 1646, 1597, 1346, 1166 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.67 (s, 3H), 1.69 (s, 3H), 2.42 (s, 3H), 3.61 (s, 2H), 3.77 (s, 2H), 4.84 (s, 1H), 4.93 (s, 1H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.66 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 13.0 (CH_3), 17.4 (CH_3), 21.5 (CH_3), 49.6 (CH_2), 50.1 (CH_2), 108.6 (CH_2), 125.9 (C), 127.9 (CH × 2), 128.3 (C), 129.5 (CH × 2), 133.4 (C), 138.9 (C), 143.5 (C).



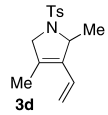
4b

3-Methyl-1-(4-toluenesulfonyl)-4-vinyl-2,5-dihydro-1*H*-pyrrole (3c): Colorless solid; IR (film): ν = 1596, 1336, 1161 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.70 (s, 3H), 2.43 (s, 3H), 4.07 (s, 1H), 4.20 (s, 2H), 4.96 (d, *J* = 17.6 Hz, 1H), 5.12 (d, *J* = 10.8 Hz, 1H), 6.43 (dd, *J* = 10.8, 17.6 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 11.4 (CH_3), 21.5 (CH_3), 54.7 (CH_2), 59.2 (CH_2), 115.2 (CH_2), 127.5 (CH × 2), 127.6 (CH), 129.4 (C), 129.8 (CH × 2), 131.6 (C), 134.1 (C), 143.4 (C); LRMS: *m/z* = 263 (M^+), 248, 236, 155, 108, 91; HRMS: *m/z* calcd. for $C_{14}H_{17}NO_2S$ (M^+): 263.0987; found: 263.0982.



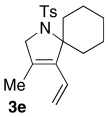
3c

2,4-Dimethyl-1-(4-toluenesulfonyl)-3-vinyl-2,5-dihydro-1*H*-pyrrole (3d): Colorless oil; IR (neat): ν = 1662, 1599, 1342, 1162 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.46 (d, *J* = 6.8 Hz, 3H), 1.65 (s, 3H), 2.40 (s, 3H), 4.00 (d, *J* = 15.6 Hz, 1H), 4.12 (dd, *J* = 3.2, 15.6 Hz, 1H), 4.74 (m, 1H), 5.04 (d, *J* = 17.6 Hz, 1H), 5.15 (d, *J* = 11.2 Hz, 1H), 6.31 (dd, *J* = 11.2, 17.6 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 11.4 (CH_3), 21.4 (CH_3), 22.0 (CH_3), 58.2 (CH_2), 63.0 (CH), 115.5 (CH_2), 127.2 (CH × 2), 127.4 (CH), 129.6 (CH × 2), 130.7 (C), 134.4 (C), 135.3 (C), 143.2 (C); LRMS: *m/z* = 277 (M^+), 262, 250, 155, 122, 106, 91; HRMS: *m/z* calcd. for $C_{15}H_{19}NO_2S$ (M^+): 277.1137; found: 277.1143.



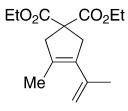
3d

3-Methyl-1-(4-toluenesulfonyl)-4-vinyl-1-azaspiro[4.5]dec-3-ene (3e): Colorless oil; IR (neat): ν = 1654, 1598, 1366, 1157 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34 – 1.68 (m, 6H), 1.67 (s, 3H), 1.83 (d, *J* = 12.8 Hz, 2H), 2.41 (s, 3H), 2.62 (dt, *J* = 6.0, 12.8 Hz, 2H), 3.94 (s, 2H), 5.06 (dd, *J* = 2.4, 17.6 Hz, 1H), 5.30 (dd, *J* = 2.4, 11.2 Hz, 1H), 6.30 (dd, *J* = 11.2, 17.6 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 12.7 (CH_3), 21.4 (CH_3), 23.6 (CH_2 × 2), 24.4 (CH_2), 36.3 (CH_2 × 2), 57.6 (CH_2), 76.6 (C), 119.4 (CH_2), 127.1 (C), 127.2 (CH × 2), 129.3 (CH × 2), 132.4 (CH), 138.7 (C), 141.2 (C), 142.6 (C); LRMS: *m/z* = 331 (M^+), 316, 302, 288, 275, 211, 176, 155, 120, 91; HRMS: *m/z* calcd. for $C_{19}H_{25}NO_2S$ (M^+): 331.1601; found: 331.1612.



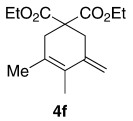
3e

Diethyl 3-isopropenyl-4-methylcyclopent-3-ene-1,1-dicarboxylate (3f): Colorless oil; IR (neat): ν = 1734 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.3 Hz, 6H), 1.79 (br s, 3H), 1.90 (s, 3H), 3.03 (s, 2H), 3.13 (q, *J* = 1.9 Hz, 2H), 4.19 (q, *J* = 7.3 Hz, 4H), 4.80 (s, 1H), 4.93 (s, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 14.0 (CH_3 × 2), 15.2 (CH_3), 22.5 (CH_3), 43.6 (CH_2), 47.1 (CH_2), 56.9 (C), 61.5 (CH_2 × 2), 114.0 (CH_2), 131.5 (C), 133.1 (C), 140.4 (C), 172.3 (C × 2); LRMS: *m/z* = 266 (M^+), 221, 192, 177, 163, 147, 133, 119; HRMS: *m/z* calcd. for $C_{15}H_{22}O_4$ (M^+): 266.1518; found: 266.1520.

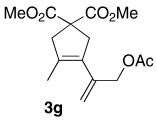


3f

Diethyl 3,4-dimethyl-5-methylenecyclohex-3-ene-1,1-dicarboxylate (4f): Colorless oil; IR (neat): ν = 1736, 1640, 1611, 1248 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.22 (t, *J* = 7.0 Hz, 6H), 1.76 (s, 3H), 1.80 (s, 3H), 2.62 (br s, 2H), 2.84 (s, 2H), 4.12 – 4.20 (m, 4H), 4.80 (s, 1H), 4.93 (s, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 13.8 (CH_3), 14.0 (CH_3 × 2), 20.2 (CH_3), 37.5 (CH_2), 37.8 (CH_2), 54.1 (C), 61.3 (CH_2 × 2), 109.1 (CH_2), 126.1 (C), 130.3 (C), 141.3 (C), 171.0 (C × 2); LRMS: *m/z* = 266 (M^+), 221, 193, 165, 147, 133, 119; HRMS: *m/z* calcd. for $C_{15}H_{22}O_4$ (M^+): 266.1518; found: 266.1514.

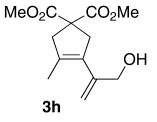


4f



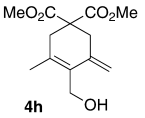
3g

Dimethyl 3-(1-acetoxymethylvinyl)-4-methylcyclopent-3-ene-1,1-dicarboxylate (3g): Colorless oil; IR (neat): $\nu = 1738, 1637, 1435, 1255, 1199, 1167, 1072\ cm^{-1}$; ^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.76$ (s, 3H), 2.08 (s, 3H), 3.06 (s, 2H), 3.14 (m, 2H), 3.74 (s, 6H), 4.64 (s, 2H), 5.05 (s, 1H), 5.27 (s, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 14.9$ (CH_3), 20.9 (CH_3), 43.5 (CH_2), 46.9 (CH_2), 52.8 ($CH_3 \times 2$), 57.0 (C), 65.8 (CH_2), 116.2 (CH_2), 130.2 (C), 133.7 (C), 139.1 (C), 170.6 (C), 172.5 (C × 2); LRMS: $m/z = 296$ (M^+), 254, 236, 221, 204, 194, 177, 172, 117; HRMS: m/z calcd. for $C_{15}H_{20}O_6$ (M^+): 296.1260; found: 296.1246.



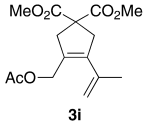
3h

Dimethyl 3-(1-hydroxymethylvinyl)-4-methylcyclopent-3-ene-1,1-dicarboxylate (3h): Colorless oil; IR (neat): $\nu = 3537, 1732, 1436, 1260, 1200, 1168, 1072\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.78$ (s, 3H), 3.06 (s, 2H), 3.12 (m, 2H), 3.73 (s, 6H), 4.22 (s, 2H), 4.97 (s, 1H), 5.26 (s, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 14.9$ (CH_3), 43.3 (CH_2), 46.8 (CH_2), 52.8 ($CH_3 \times 2$), 57.2 (C), 65.1 (CH_2), 113.7 (CH_2), 130.7 (C), 133.7 (C), 144.0 (C), 172.5 (C × 2); LRMS: $m/z = 254$ (M^+), 236, 223, 204, 194, 176, 145, 117; HRMS: m/z calcd. for $C_{13}H_{18}O_5$ (M^+): 254.1154; found: 254.1166.



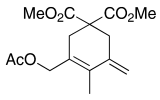
4h

Dimethyl 4-hydroxymethyl-3-methyl-5-methylenecyclohex-3-ene-1,1-dicarboxylate (4h): Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.91$ (s, 3H), 2.67 (s, 2H), 2.87 (s, 2H), 3.70 (s, 6H), 4.35 (s, 2H), 4.94 (s, 1H), 5.16 (s, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 19.7$ (CH_3), 37.5 (CH_2), 37.9 (CH_2), 52.7 ($CH_3 \times 2$), 53.9 (C), 57.9 (CH_2), 110.0 (CH_2), 130.2 (C), 135.2 (C), 138.6 (C), 171.1 (C × 2); LRMS: $m/z = 236$ ($M^+ - H_2O$), 193, 176, 165, 145, 117.



3i

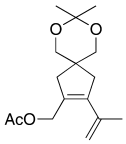
Dimethyl 3-acetoxymethyl-4-isopropenylcyclopent-3-ene-1,1-dicarboxylate (3i): colorless oil; IR (neat): $\nu = 1740, 1636, 1603, 1230\ cm^{-1}$; ^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.86$ (s, 3H), 2.06 (s, 3H), 3.15 (s, 2H), 3.18 (m, 2H), 3.75 (s, 6H), 4.73 (s, 2H), 4.81 (s, 1H), 5.02 (s, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 20.9$ (CH_3), 21.9 (CH_3), 42.7 (CH_2), 43.5 (CH_2), 52.9 ($CH_3 \times 2$), 57.0 (C), 60.8 (CH_2), 116.0 (CH_2), 129.3 (C), 139.2 (C), 139.8 (C), 170.9 (C), 172.3 (C × 2); LRMS: $m/z = 296$ (M^+), 236, 204, 191, 177, 145, 131, 117; HRMS: m/z calcd. for $C_{15}H_{20}O_6$ (M^+): 296.1260; found: 296.1251.



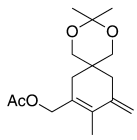
4i

Dimethyl 3-acetoxymethyl-4-methyl-5-methylenecyclohex-3-ene-1,1-dicarboxylate (4i): colorless oil; IR (neat): $\nu = 1738, 1640, 1610, 1230\ cm^{-1}$; ^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.85$ (s, 3H), 2.08 (s, 3H), 2.73 (s, 2H), 2.88 (s, 2H), 3.70 (s, 6H), 4.71 (s, 2H), 4.99 (s, 1H), 5.13 (s, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 13.7$ (CH_3), 20.9 (CH_3), 34.2 (CH_2), 37.2 (CH_2), 52.7 ($CH_3 \times 2$), 53.8 (C), 64.6 (CH_2), 112.8 (CH_2), 127.9 (C), 131.1 (C), 140.6 (C), 171.0 (C), 171.1 (C × 2); LRMS: $m/z = 296$ (M^+), 254, 236, 223, 204, 177, 163, 117; HRMS: m/z calcd. for $C_{15}H_{20}O_6$ (M^+): 296.1260; found: 296.1258.

3-Isopropenyl-8,8-dimethyl-7,9-dioxaspiro[4.5]dec-2-en-2-ylmethyl acetate (3j) and 3,3,9-trimethyl-10-methylene-2,4-dioxaspiro[5.5]undec-8-en-8-ylmethyl acetate (4j): ^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.41$ (s, 3 + 3 H), 1.43 (s, 3 + 3 H), 1.84 (s, 3H), 1.85 (s, 3H), 2.04 (s, 3H), 2.06 (s, 3H), 2.16 (br, 2H), 2.29 (br, 2H), 2.37 (br, 2H), 2.54 (br, 2H), 3.53 (s, 4H), 3.67 (s, 4H), 4.67 (s, 2H), 4.71 (s, 2H), 4.76 (s, 1H), 4.95 (s, 1H), 4.97 (s, 1H) 5.11 (s, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 13.7$ (CH_3), 20.9 (CH_3), 22.1 ($CH_3 \times 2$), 23.5 ($CH_3 \times 2$), 24.0 (CH_3), 24.2 (CH_3), 32.2 (C), 35.2 (CH_2), 37.8 (CH_2), 38.6 (C), 42.3 (CH_2), 43.3 (CH_2), 61.4 (CH_2), 65.1 (CH_2), 68.1 ($CH_2 \times 2$), 69.1 ($CH_2 \times 2$), 97.8 (C), 98.2 (C), 112.5 (CH_2), 115.1 (CH_2), 128.0 (C), 130.1 (C), 131.2 (C), 140.2 (C), 141.0 (C), 141.6 (C), 170.9 (C), 171.1 (C).

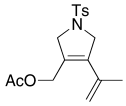


3j

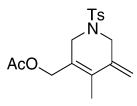


4j

4,4-Bis(benzyloxymethyl)-2-isopropenylcyclopent-1-enylmethyl acetate (3k) and 5,5-bis(benzyloxymethyl)-2-methyl-3-methylenecyclohex-1-enylmethyl acetate (4k): ^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.82$ (s, 3H), 1.85 (s, 3H), 2.00 – 2.05 (m, 3 + 3H), 2.18 (s, 2H), 2.36 (s, 2H), 2.39 (s, 2H), 2.44 (s, 2H), 3.35 (s, 4H), 3.45 (s, 4H), 4.48 (s, 4H), 4.53 (s, 4H), 4.64 (s, 2H), 4.71 (s, 2H), 4.74 (s, 1H), 4.89 (s, 1H), 4.95 (s, 1H), 5.06 (s, 1H), 7.24 – 7.32 (m, 10 + 10H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 13.5$ (CH_3), 20.8 ($CH_3 \times 2$), 22.0 (CH_3), 33.5 (CH_2), 36.9 (CH_2), 38.6 (C), 41.5 (CH_2), 42.4 (CH_2), 44.7 (C), 61.5 (CH_2), 65.1 (CH_2), 73.1 ($CH_2 \times 4$), 73.2 ($CH_2 \times 2$), 74.0 ($CH_2 \times 2$), 111.5 (CH_2), 114.7 (CH_2), 127.2 (CH × 5), 127.3 (CH × 5), 128.1 (CH × 5), 128.2 (CH × 5), 128.5 (C), 130.4 (C), 130.7 (C), 138.7 (C × 2), 138.8 (C × 2), 140.3 (C), 141.0 (C), 142.6 (C), 170.8 (C), 171.0 (C).



3k



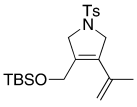
4k

4-Isopropenyl-1-(4-toluenesulfonyl)-2,5-dihydro-1*H*-pyrrol-3-ylmethyl acetate (3l) and 4-methyl-5-methylene-1-(4-toluenesulfonyl)-1,2,5,6-tetrahydropyridin-3-ylmethyl acetate (4l): ^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.75$ (s, 3H), 1.83 (s, 3H), 2.04 (s, 3H), 2.07 (s, 3H), 2.42 (s, 3H), 2.44 (s, 3H), 3.78 (s, 2H), 3.81 (s, 2H), 4.22 (br, 4H), 4.61 (s, 2H), 4.70 (s, 2H), 4.80 (s, 1H) 5.01 (s, 1H), 5.06 (s, 1H) 5.11 (s, 1H), 7.31 (d, $J = 8.4$ Hz, 2H), 7.34 (d, $J = 8.4$ Hz, 2H), 7.65 (d, $J = 8.4$ Hz, 2H), 7.71 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 12.9$ (CH_3), 20.6 (CH_3), 20.7 (CH_3), 21.4 (CH_3 x 2), 21.8 (CH_3), 47.4 (CH_2), 49.3 (CH_2), 56.6 (CH_2), 56.8 (CH_2), 58.9 (CH_2), 62.3 (CH_2), 111.8 (CH_2), 117.4 (CH_2), 126.5 (C), 127.4 (CH × 2), 127.8 (CH × 2), 129.4 (CH × 2), 129.6 (C), 129.7 (CH × 2), 130.8 (C), 133.4 (C), 133.9 (C), 136.5 (C), 136.8 (C), 138.1 (C), 143.5 (C × 2), 170.4 (C), 170.6 (C).

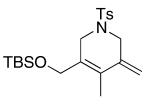
3l

4l

3-(*tert*-Butyldimethylsiloxymethyl)-4-isopropenyl-1-(4-toluenesulfonyl)-2,5-dihydro-1*H*-pyrrole (3m) and 5-(*tert*-butyldimethylsiloxymethyl)-4-methyl-3-methylene-1-(4-toluenesulfonyl)-1,2,3,6-tetrahydropyridine (4m): ^1H NMR (270 MHz, $CDCl_3$): $\delta = 0.00$ (s, 6H), 0.05 (s, 6H), 0.85 (s, 9H), 0.89 (s, 9H), 1.65 (s, 3H), 1.79 (s, 3H), 2.40 (s, 3H), 2.42 (s, 3H), 3.77 (s, 2H), 4.22 – 4.28 (m, 10H), 4.67 (s, 1H), 4.92 (s, 1H), 4.99 (s, 1H), 4.99 (s, 1H), 7.26 (d, $J = 8.1$ Hz, 2H), 7.31 (d, $J = 8.1$ Hz, 2H), 7.66 (d, $J = 8.1$ Hz, 2H), 7.72(d, $J = 8.1$ Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 12.9$ (CH_3), 20.6 (CH_3), 20.7 (CH_3), 21.4 ($CH_3 \times 2$), 21.8 (CH_3), 47.4 (CH_2), 49.3 (CH_2), 56.6 (CH_2), 56.8 (CH_2), 58.9 (CH_2), 62.3 (CH_2), 111.8 (CH_2), 117.4 (CH_2), 126.5 (C), 127.4 (CH × 2), 127.8 (CH × 2), 129.4

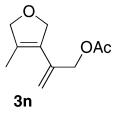


3m

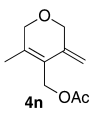


4m

(CH × 2), 129.6 (C), 129.7 (CH × 2), 130.8 (C), 133.4 (C), 133.9 (C), 136.5 (C), 136.8 (C), 138.1 (C), 143.5 (C × 2), 170.4 (C), 170.6 (C).



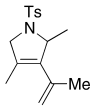
3n



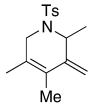
4n

2-(4-Methyl-2,5-dihydrofuran-3-yl)allyl acetate (3n): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.79 (s, 3H), 2.09 (s, 3H), 4.62 (br, 2H), 4.70 (s, 2H), 4.75 (br, 2H), 5.02 (s, 1H), 5.29 (s, 1H); LRMS: *m/z* = 182 (M^+), 122, 43.

5-Methyl-3-methylene-3,6-dihydro-2*H*-pyran-4-ylmethyl acetate (4n): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.80 (s, 3H), 2.05 (s, 3H), 4.14 (s, 2H), 4.23 (s, 2H), 4.81 (s, 1H), 4.85 (s, 2H), 5.00 (s, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 14.9 (CH_3), 20.9 (CH_3), 58.7 (CH_2), 70.0 (CH_2), 70.1 (CH_2), 106.5 (CH_2), 124.4 (C), 138.3 (C), 138.6 (C), 171.1 (C); LRMS: *m/z* = 182 (M^+), 122, 109, 43.



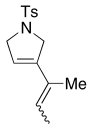
3o



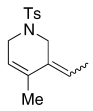
4o

3-Isopropenyl-2,4-dimethyl-1-(4-toluenesulfonyl)-2,5-dihydro-1*H*-pyrrole (3o): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (d, *J* = 6.0 Hz, 3H), 1.62 (s, 3H), 1.69 (s, 3H), 2.42 (s, 3H), 3.97 (d, *J* = 14.8 Hz, 1 H), 4.09 (dd, *J* = 4.8, 14.8 Hz, 1H), 4.58 (m, 1H), 4.74 (s, 1H), 5.04 (s, 1H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.72 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 12.3 (CH_3), 21.4 (CH_3), 21.5 (CH_3), 21.8 (CH_3), 58.8 (CH_2), 64.8 (CH), 116.4 (CH_2), 126.5 (C), 127.2 (CH × 2), 129.5 (CH × 2), 135.1 (C), 137.4 (C), 137.9 (C), 143.1 (C); LRMS: *m/z* = 291 (M^+), 276 (M^+ – Me), 249, 155, 135, 120.

2,4,5-Trimethyl-3-methylene-1-(4-toluenesulfonyl)-1,2,3,6-tetrahydropyridine (4o): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.19 (d, *J* = 7.2 Hz, 3H), 1.54 (s, 3H), 1.63 (s, 3H), 2.38 (s, 3H), 3.72 (d, *J* = 18.8 Hz, 1H), 3.97 (d, *J* = 18.8 Hz, 1H), 4.63 (q, *J* = 7.2 Hz, 1H), 4.74 (s, 1H), 4.78 (s, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 13.0 (CH_3), 16.9 (CH_3), 19.9 (CH_3), 21.3 (CH_3), 45.3 (CH_2), 53.8 (CH), 107.8 (CH_2), 124.2 (C), 126.8 (C), 127.2 (CH × 2), 129.0 (CH × 2), 136.6 (C), 142.8 (C), 143.4 (C); LRMS: *m/z* = 291 (M^+), 276, 155, 135, 120.

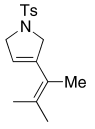


3q

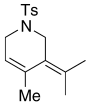


4q

3-(1-Methylpropenyl)-1-(4-toluenesulfonyl)-2,5-dihydro-1*H*-pyrrole (3q) and 3-ethylidene-4-methyl-1-(4-toluenesulfonyl)-1,2,3,6-tetrahydropyridine (4q): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.56 (s, 3H), 1.73 (s, 3H), 1.64 – 1.94 (m, 18H), 2.42 (s, 3 + 3H), 2.43 (s, 3 + 3H), 3.62 (s, 2.3/4H), 3.70 (s, 4H), 3.87 (s, 1.7/4H), 4.18 (m, 4H), 4.22 (m, 2/4H), 4.28 (m, 2/4H), 5.35-5.46 (m, 8H), 7.27 – 7.34 (m, 8H), 7.64 – 7.75 (m, 8H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 13.1 (CH_3), 13.2 (CH_3), 13.8 (CH_3), 14.8 (CH_3), 14.9 (CH_3), 18.8 (CH_3), 21.5 (CH_3 × 4), 23.1 (CH_3 x 2), 43.9 (CH_2), 45.1 (CH_2), 45.9 (CH_2), 52.3 (CH_2), 54.3 (CH_2), 54.4 (CH_2), 55.3 (CH_2), 55.9 (CH_2), 117.4 (CH), 119.2 (CH), 120.4 (CH), 121.3 (CH), 122.4 (CH), 124.4 (CH), 124.5 (CH), 125.1 (CH), 127.4 (CH × 4), 127.7 (CH × 2), 127.8 (CH x 2), 127.9 (C), 128.6 (C), 129.3 (CH × 2), 129.4 (CH x 2), 129.6 (C), 129.7 (CH × 4), 130.0 (C), 131.0 (C), 132.4 (C), 132.7 (C), 133.8 (C), 133.9 (C), 134.2 (C), 134.3 (C), 138.1 (C), 140.2 (C), 143.3 (C), 143.4 (C), 143.4 (C).

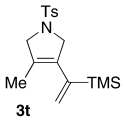


3r



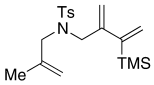
4r

3-(1,2-Dimethylpropenyl)-1-(4-toluenesulfonyl)-2,5-dihydro-1*H*-pyrrole (3r) and 3-isopropylidene-4-methyl-1-(4-toluenesulfonyl)-1,2,3,6-tetrahydropyridine (4r): ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.60 (s, 3H), 1.62 (m, 3H), 1.67 (s, 3H), 1.77 (s, 3H), 1.80 (s, 3H), 1.89 (m, 3H), 2.41 (s, 3H), 2.42 (s, 3H), 3.76 (br s, 2H), 3.79 (s, 2H), 4.10 – 4.18 (m, 4H), 5.26 (m, 1H), 5.30 (m, 1H), 7.27 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.64 (d, *J* = 8.1 Hz, 2H), 7.73 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 17.6 (CH_3), 20.6 (CH_3), 21.4 (CH_3), 21.9 (CH_3), 22.6 (CH_3), 23.1 (CH_3), 24.1 (CH_3), 45.9 (CH_2), 46.3 (CH_2), 54.9 (CH_2), 56.1 (CH_2), 120.0 (CH), 121.3 (CH), 122.1 (C), 125.2 (C), 127.3 (CH × 2), 127.5 (CH × 2), 129.2 (CH × 2), 129.6 (CH × 2), 130.4 (C), 130.9 (C), 134.0 (C), 134.2 (C), 134.5 (C), 140.6 (C), 143.1 (C), 143.3(C).



3t

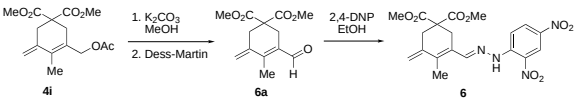
3-Methyl-1-(4-toluenesulfonyl)-4-[1-(trimethylsilyl)vinyl]-2,5-dihydro-1*H*-pyrrole (3t): Colorless oil; IR (neat): ν = 1654, 1598, 1444, 1349, 1250, 1164, 1099 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.02 (s, 9H), 1.52 (s, 3H), 2.43 (s, 3H), 4.05 (s, 2H), 4.05 (s, 2H), 5.50 (d, *J* = 3.6 Hz, 1H), 5.54 (d, *J* = 3.6 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = −1.3 (CH_3 × 3), 12.0 (CH_3), 21.5 (CH_3), 58.5 (CH_2), 59.0 (CH_2), 125.6 (C), 127.4 (CH × 2), 129.1 (CH_2), 129.7 (CH × 2), 134.2 (C), 134.5 (C), 143.3 (C), 146.4 (C); LRMS: *m/z* = 335 (M^+), 320, 236, 180, 155, 139; anal. calcd. for $C_{17}H_{25}NO_2SSi$: C 60.85, H 7.51, N 4.17, S 9.56%; found: C 60.76, H 7.44, N 4.12, S 9.68%.



7t

4-Methyl-*N*-(2-methylallyl)-*N*-[2-methylene-3-(trimethylsilyl)-but-3-enyl]benzenesulfonamide (7t): Colorless oil; IR (neat): ν = 1654, 1598, 1495, 1445, 1343, 1160 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.11 (s, 9H), 1.60 (s, 3H), 2.42 (s, 3H), 3.76 (s, 2H), 3.89 (s, 2H), 4.76 (s, 1H), 4.84 (s, 1H), 4.89 (s, 1H), 4.91 (s, 1H), 5.43 (d, *J* = 2.2 Hz, 1H), 5.68 (d, *J* = 2.2 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = −0.9 (CH_3 × 3), 20.0 (CH_3), 21.5 (CH_3), 50.7 (CH_2), 53.2 (CH_2), 113.7 (CH_2), 114.4 (CH_2), 126.7 (CH_2), 127.3 (CH × 2), 129.5 (CH x 2), 137.6 (C), 140.1 (C), 143.0 (C), 144.2 (C), 150.5 (C); LRMS: *m/z* = 363 (M^+), 348, 334, 307, 292, 276, 208, 192, 155, 91; HRMS: *m/z* calcd. for $C_{19}H_{29}NO_2SSi$: 363.1688; found: 363.1680.

Synthesis of Compounds 6



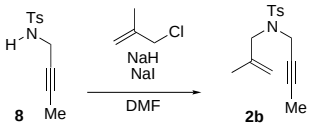
4i 6a 6 (1)

Dimethyl 3-hydroxymethyl-4-methyl-5-methylenecyclohex-3-ene-1,1-dicarboxylate (6b): A solution of **4i** (39 mg, 0.13 mmol) in MeOH (3 mL) was treated with K_2CO_3 (20 mg, 0.14 mmol) at 0° C and the solution was stirred at room temperature for 12 h. To this solution was added saturated aqueous NH_4Cl and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated to afford **6b** as a colorless oil; yield: 33.5 mg (quant.). IR (neat): ν = 3420, 1732, 1608, 1258, 1200 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.63 (br s, 1H), 1.84 (s, 3H), 2.80 (s, 2H), 2.91 (s, 2H), 3.71 (s, 6H), 4.26 (s, 2H), 4.97 (s, 1H), 5.10 (s, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 13.3 (CH_3), 34.2 (CH_2), 37.3 (CH_2), 52.7 (CH_3 × 2), 54.0 (C), 63.0 (CH_2), 112.1 (CH_2), 129.0 (C), 132.4 (C), 140.8 (C), 171.3 (C × 2); LRMS: *m/z* = 254

(M^+), 236, 204, 195, 177, 145, 117; HRMS: *m/z* calcd. for $C_{13}H_{18}O_5$ (M^+): 254.1154; found: 254.1170.

Dimethyl 3-formyl-4-methyl-5-methylenecyclohex-3-ene-1,1-dicarboxylate (6a): To a suspension of Dess–Martin periodinane (67 mg, 0.16 mmol) in CH_2Cl_2 (0.3 mL) was added a solution of **6b** (29 mg, 0.11 mmol) in CH_2Cl_2 (0.7 mL) at 0° C, and the solution was stirred at room temperature for 30 min. To this solution was added saturated aqueous $NaHCO_3$ and $Na_2S_2O_3$, and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography on silica gel (hexane/ether, 2:1) to afford **6a** as a slightly yellow oil; yield: 25.5 mg (89%). IR (neat): $\nu = 1732$, 1660, 1594, 1382, 1258 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.27$ (m, 3H), 2.87 (s, 2H), 2.93 (s, 2H), 3.70 (s, 6H), 5.35 (s, 1H), 5.62 (s, 1H), 10.28 (s, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 12.3$ (CH_3), 29.2 (CH_2), 36.9 (CH_2), 52.8 ($CH_3 \times 2$), 53.0 (C), 118.8 (CH_2), 132.1 (C), 141.2 (C), 146.6 (C), 170.8 ($C \times 2$), 190.8 (CH); LRMS: $m/z = 252$ (M^+), 235, 221, 193, 161, 133, 105; HRMS: *m/z* calcd. for $C_{13}H_{16}O_5$ (M^+): 252.0998; found: 252.1002.

Dimethyl 3-[(2,4-dinitrophenyl)-hydrazonomethyl]-4-methyl-5-methylenecyclohex-3-ene-1,1-dicarboxylate (6): To a suspension of **6a** (25.5 mg, 0.1 mmol) in EtOH (1.0 mL) was added a solution of 2,4-DNP (0.1 mmol, 0.25 M solution) in phosphoric acid/EtOH (0.4 mL), and the solution was stirred at room temperature for 10 min. The solution was diluted with ether, and the organic layer was washed with water, 10% aqueous HCl, brine, dried over Na_2SO_4, and evaporated. The crude product (40 mg, quant.) was recrystallized from ethyl acetate to yield **6** as red crystals; mp (AcOEt) 212–215° C. IR (nujol): $\nu = 1730$, 1614, 1595, 1515, 1456, 1331 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.09$ (s, 3H), 2.98 (s, 2H), 3.13 (s, 2H), 3.75 (s, 6H), 5.21 (s, 1H), 5.41 (s, 1H), 8.01 (d, $J = 9.6$ Hz, 1H), 8.31 (s, 1H), 8.34 (dd, $J = 9.6$, 2.4 Hz, 1H), 9.14 (d, $J = 2.4$ Hz, 1H) 11.29 (s, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 13.6$ (CH_3), 30.9 (CH_2), 37.1 (CH_2), 52.9 ($CH_3 \times 2$), 53.4 (C), 116.0 (CH_2), 117.0 (CH), 123.4 (CH), 128.1 (C), 129.4 (C), 130.0 (CH), 138.0 (C), 138.3 (C), 140.8 (C), 144.6 (C), 146.8 (CH), 171.1 ($C \times 2$); LRMS: $m/z = 432$ (M^+), 385, 373, 341, 313, 266, 252, 158, 130; HRMS: *m/z* calcd. for $C_{19}H_{20}N_4O_8$ (M^+): 432.1281; found: 432.1291.



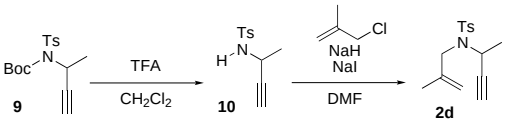
(2)

Synthesis of *N*-But-2-ynyl-4-methyl-*N*-(2-methylallyl)benzenesulfonamide (2b)

To a suspension of NaH (108 mg, 2.7 mmol) in THF/DMF (1/2, 12 mL) was added **8** (504 mg, 2.3 mmol) at 0° C, and the solution was stirred at 0° C for 1 h. To this solution was added methallyl chloride (0.26 mL, 2.7 mmol) and NaI (405 mg, 2.7 mmol). The whole solution was stirred at room temperature for 9 h. To this solution was added saturated aqueous NH_4Cl and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography on silica gel (hexane/AcOEt 9:1) to afford **2b** as a colorless solid; yield: 620 mg (quant.). IR (nujol): $\nu = 2224$, 1655, 1360, 1158, 904 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): $\delta =$ 1.51 (t, $J = 2.3$ Hz, 6H), 1.76 (s, 3H), 2.42 (s, 3H), 3.70 (s, 2H), 3.97 (q, $J = 2.3$ Hz, 2H), 4.95 (s, 1H), 4.95 (s, 1H), 7.29 (d, $J =$ 8.0 Hz, 2H), 7.75 (d, $J = 8.0$ Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 3.1$ (CH_3), 19.7 (CH_3), 21.4 (CH_3), 36.0 (CH_2), 52.4 (CH_2), 71.5 (C), 81.4 (C), 115.0 (CH_2), 127.9 ($CH \times 2$), 129.1 ($CH \times 2$), 136.3 (C), 139.5 (C), 143.1 (C); LRMS: $m/z = 277$ (M^+), 262, 236, 184, 155, 122; HRMS: *m/z* calcd. for $C_{15}H_{19}NO_2S$ (M^+): 277.1136; found: 277.1133.

Synthesis of 2c

Enyne **2c** was prepared according to the literature procedure.[10]



(3)

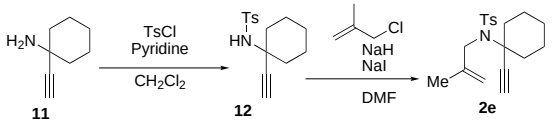
Synthesis of 2d

Sulfonamide **9** was prepared according to the literature procedure.[11]

4-Methyl-*N*-(1-methylprop-2-ynyl)-benzenesulfonamide (10): To a solution of **9** (1.0 g, 3.2 mmol) in CH_2Cl_2 (16 mL) was added trifluoroacetic acid (1.2 mL, 15.9 mmol) at 0° C and the solution was stirred at room temperature for 4.5 h. To this solution was added saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The resulting crude product (amorphous solid, yield: 692 mg, 97%) was used without further purification. IR (nujol): $\nu = 3264$, 2110, 1654, 1599, 1329, 1163 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.43$ (d, $J = 7.3$ Hz, 3H), 2.09 (d, $J =$ 2.2 Hz, 1H), 2.43 (s, 3H), 4.11-4.25 (m, 1 H), 4.58 (br, 1 H), 7.30 (d, $J = 8.1$ Hz, 2 H), 7.78 (d, $J = 8.1$ Hz, 2 H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 21.4$ (CH_3), 23.1 (CH_3), 41.0 (CH), 71.7 (CH), 82.7 (C), 127.3 ($CH \times 2$), 129.4 ($CH \times 2$), 137.2 (C), 143.4 (C); LRMS: $m/z = 223$ (M^+), 208, 155, 91; HRMS: *m/z* calcd. for $C_{11}H_{13}NO_2S$ (M^+): 223.0667; found: 223.0676.

4-Methyl-*N*-(2-methylallyl)-*N*-(1-methylprop-2-ynyl)benzenesulfonamide (2d): A crude product which was prepared from **10** (668 mg, 3.0 mmol), methallyl chloride (0.6 mL, 6.0 mmol), NaI (1.0 g, 6.7 mmol), and NaH (154 mg, 3.6 mmol), according to the procedure for the synthesis of **2b**, was purified by column chromatography on silica gel (hexane/AcOEt, 5:1) to afford **2d** as colorless crystals; yield: 820 mg (99%). Mp (ether/hexane) 84–85.5° C; IR (nujol): $\nu = 2111$, 1655, 1597, 1162 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.43$ (d, $J = 6.8$ Hz, 3H), 1.82 (s, 3H), 2.11 (d, $J = 2.0$ Hz, 1H), 2.42 (s, 3H), 3.65 (d, $J = 16.0$ Hz, 1H), 3.88 (dd, $J = 16.0$, 1.0 Hz, 1H), 4.86–4.91 (m, 2H), 5.04 (s, 1H), 7.29 (d, $J = 8.4$ Hz, 2H), 7.71 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 19.9$ (CH_3), 21.5 (CH_3), 22.3 (CH_3), 46.5 (CH), 50.9 (CH_2), 73.5 (CH), 80.8

(C), 113.3 (CH_2), 127.6 (CH × 2), 129.4 (CH × 2), 136.0 (C), 142.4 (C), 143.3 (C); LRMS: $m/z = 277$ (M^+), 262, 236, 212, 198, 184, 155, 122, 106, 91; anal. calcd. for $C_{15}H_{19}NO_2S$: C 64.95, H 6.90, N 5.05, S 11.56%; found: C 64.96, H 7.03, N 5.05, S 11.49%.

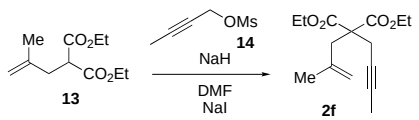


(4)

Synthesis of 2e

***N*-(1-Ethynylcyclohexyl)-4-methylbenzenesulfonamide (12):** To a solution of **11** (1.35 mL, 10 mmol) in CH_2Cl_2 (10 mL) was added pyridine (2.4 mL, 30 mmol) and *p*-toluenesulfonyl chloride (TsCl, 2.0 g, 10.5 mmol) at 0° C, and the solution was stirred at room temperature for 23 h. The solvent was removed and the residue was dissolved in ethyl acetate. The organic layer was washed with aqueous 10% HCl and brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography on silica gel (hexane/AcOEt, 5:1) to afford **12** as an amorphous solid; yield: 2.1 g (74%). IR (nujol): ν = 3258, 1601, 1338, 1151 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ = 1.18 – 1.69 (m, 8H), 1.98 – 2.03 (m, 2H), 2.12 (s, 1H), 2.41 (s, 3H), 4.99 (br, 1H), 7.26 (d, $J = 8.1$ Hz, 2H), 7.80 (d, $J = 8.1$ Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 21.5 (CH_3), 22.3 (CH_2 × 2), 24.8 (CH_2), 38.7 (CH_2 × 2), 54.3 (C), 73.7 (CH), 83.8 (C), 127.6 (CH × 2), 129.1 (CH × 2), 139.2 (C), 143.0 (C); LRMS: m/z = 277 (M^+), 234, 184, 170, 155, 122, 106, 91; HRMS: m/z calcd. for $C_{15}H_{19}NO_2S$ (M^+): 277.1136; found: 277.1131.

***N*-(1-Ethynylcyclohexyl)-4-methyl-*N*-(2-methylallyl)benzenesulfonamide (2e):** A crude product which was prepared from **12** (610 mg, 2.2 mmol), methallyl chloride (0.32 mL, 3.3 mmol), NaI (485 mg, 3.3 mmol), and NaH (135 mg, 3.3 mmol), according to the procedure for the synthesis of **2b**, was purified by column chromatography on silica gel (hexane/AcOEt, 5:1) to afford **2e** as colorless crystals; yield: 722 mg (99%). Mp (ether/hexane) 97.5 – 99.5° C; IR (nujol): ν = 2100, 1655, 1598, 1332, 1157 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.48 – 1.66 (m, 6H), 1.80 (s, 3H), 1.88 (dt, $J = 3.6$, 12.8 Hz, 2H), 2.07 (d, $J = 10.8$ Hz, 2H), 2.24 (s, 1H), 2.41 (s, 3H), 4.12 (s, 2H), 4.94 (m, 1H), 5.12 (s, 1H), 7.25 (d, $J = 8.4$ Hz, 2H), 7.72 (d, J = 8.4 Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 20.3 (CH_3), 21.5 (CH_3), 23.5 (CH_2 × 2), 24.7 (CH_2), 37.7 (CH_2 × 2), 53.5 (CH_2), 62.4 (C), 74.9 (CH), 83.2 (C), 111.9 (CH_2), 127.5 (CH × 2), 129.2 (CH × 2), 139.5 (C), 142.9 (C), 143.3 (C); LRMS: m/z = 330 (M^+ – H), 316, 302, 288, 275, 266, 260, 252, 238, 224, 210, 196, 176, 155, 106, 91; anal. calcd. for $C_{19}H_{25}NO_2S$: C 68.85, H 7.60, N, 4.23, S 9.67%; found: C 68.90, H 7.73, N 4.20, S 9.65%.

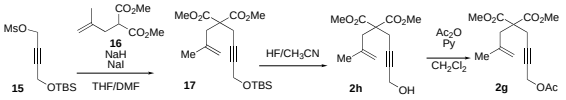


(5)

Synthesis of 2f

Malonate **13** was prepared according to the literature procedure.[12]

Diethyl 2-but-2-ynyl-2-(2-methylallyl)malonate (2f): To a suspension of NaH (200 mg, 5.0 mmol) in THF (10 mL) was added **13** (857 mg, 4.0 mmol) in DMF (5 mL) at 0° C and the solution was stirred at 0° C for 1 h. To this solution was added **14** (740 mg, 5.0 mmol) in DMF (5 mL) and NaI (749 mg, 5.0 mmol). The whole solution was stirred at room temperature for 20 h. To this solution was added saturated aqueous NH_4Cl and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography on silica gel (hexane/AcOEt, 20:1) to afford **2f** as a colorless oil; yield: 950 mg (89%). IR (neat): ν = 1736, 1644 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.0 Hz, 6H), 1.66 (s, 3H), 1.75 (t, $J = 2.4$ Hz, 3H), 2.76 (q, J = 2.4 Hz, 2H), 2.81 (s, 2H), 4.12 – 4.25 (m, 4H), 4.83 (s, 1H), 4.89 (m, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 3.4 (CH_3), 14.0 (CH_3 × 2), 22.9 (CH_2), 23.3 (CH_3), 39.4 (CH_2), 56.7 (C), 61.4 (CH_2 × 2), 73.8 (C), 78.9 (C), 115.9 (CH_2), 140.3 (C), 170.4 (C × 2); LRMS: m/z = 266 (M^+), 221, 192, 177, 147, 119; HRMS: m/z calcd. for $C_{13}H_{17}O_3$ (M^+ – EtO): 221.1178; found: 221.1173.



(6)

Synthesis of 2g and 2h

Mesylate **15** was prepared according to the literature procedure.[13] Colorless oil; IR (neat): ν = 1365, 1256, 1177, 1143, 1086, 946, 838 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ = 0.10 (s, 6H), 0.89 (s, 9H), 3.10 (s, 3H), 4.36 (t, $J = 1.8$ Hz, 2H), 4.88 (t, $J = 1.8$ Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = −5.3 (CH_3 × 2), 18.2 (C), 25.7 (CH_3 x 3), 39.0 (CH_3), 51.5 (CH_2), 57.8 (CH_2), 76.7 (C), 88.6 (C); LRMS: m/z = 221 (M^+ – Bu), 183, 167, 153.

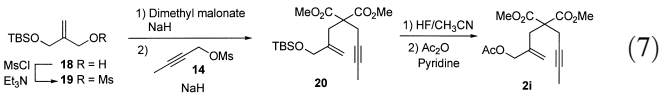
Malonate **16** was prepared according to the literature procedure.[14]

Dimethyl 2-[4-(*tert*-butyldimethylsiloxy)-but-2-ynyl]-2-(2-methylallyl)malonate (17): A crude product which was prepared from **15** (2.36 g, 8.5 mmol), **16** (1.5 g, 7.9 mmol), NaI (1.34 g, 9.0 mmol), and NaH (378 mg, 9.5 mmol), according to the procedure for the synthesis of **2f**, was purified by column chromatography on silica gel (hexane/ether, 9:1) to afford **17** as a colorless oil; yield: 2.5 g (86%). IR (neat): ν = 1741, 1645, 1252, 1209, 1078, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 0.10 (s, 6H), 0.89 (s, 9H), 1.65 (s, 3H), 2.82 (s, 2H), 2.88 (t, J = 2.2 Hz, 2H), 3.73 (s, 6H) 4.27 (t, $J = 2.2$ Hz, 2H), 4.83 (m, 1H), 4.90 (m, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = −5.3 (CH_3 × 2), 18.2 (C), 22.9 (CH_2), 23.1 (CH_3), 25.7 (CH_3 × 3), 39.5 (CH_3), 51.6 (CH_2), 52.6 (CH_3 × 2), 56.5 (C), 79.6 (C), 82.1 (C), 116.1 (CH_2), 139.8 (C), 170.5 (C × 2); LRMS: m/z = 355 (M^+ – Me), 311, 279, 221, 205, 191, 177, 161, 145; anal. calcd. for $C_{19}H_{32}O_5Si$: C 61.92, H 8.75%; found: C 61.93, H 8.80%.

Dimethyl 2-(4-hydroxybut-2-ynyl)-2-(2-methylallyl)malonate (2h): To a solution of **17** (1.9 g, 5.2 mmol) in CH_3CN (25 mL) was added HF (2.5 mL, 48% w/v in water) in CH_3CN

(22.5 mL) at 0° C and the solution was stirred at 0° C for 2 h. To this solution was added saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography on silica gel (hexane/AcOEt, 10:1 – 1:1) to afford **2h** as a colorless oil; yield: 1.34 g (quant.). IR (neat): ν = 3480, 2228, 1737, 1645, 1437, 1210, 1015 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.63 (br, 1H), 1.65 (s, 3H), 2.82 (s, 2H), 2.87 (t, J = 2.2 Hz, 2H), 3.74 (s, 6H) 4.22 (t, J = 2.2 Hz, 2H), 4.83 (m, 1H), 4.91 (m, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 23.0 (CH_2), 23.1 (CH_3), 39.6 (CH_2), 51.0 (CH_2), 52.7 ($CH_3 \times 2$), 56.6 (C), 80.7 (C), 81.9 (C), 116.3 (CH_2), 139.7 (C), 170.6 (C × 2); LRMS: m/z = 205 (M^+ – MeO–H_2O), 195, 176, 151, 145, 135, 117; anal. calcd. for $C_{13}H_{18}O_5$: C 61.40, H 7.14%; found: C 61.30, H 7.27%.

Dimethyl 2-(4-acetoxybut-2-ynyl)-2-(2-methylallyl)malonate (2g): To a solution of **2h** (509 mg, 2.0 mmol) in CH_2Cl_2 (10 mL) was added pyridine (0.3 mL, 4.0 mmol) and acetic anhydride (Ac_2O, 0.3 mL, 3.0 mmol) at 0° C and the solution was stirred at room temperature for 9 h. To this solution was added saturated aqueous NH_4Cl and the aqueous layer was extracted with ether. The organic layer was washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate, 5:1) to afford **2g** as a colorless oil; yield: 575 mg (97%). IR (neat): ν = 1738, 1645, 1437, 1212, 1026 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.64 (s, 3H), 2.07 (s, 3H), 2.81 (s, 2H), 2.87 (m, 2H), 3.73 (s, 6H), 4.61 (m, 2H), 4.82 (s, 1H), 4.90 (s, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 20.7 (CH_3), 22.9 (CH_2), 33.1 (CH_3), 39.7 (CH_2), 52.3 (CH_2), 52.7 ($CH_3 \times 2$), 56.4 (C), 77.5 (C), 82.0 (C), 116.3 (CH_2), 139.7 (C), 170.1 (C), 170.5 (C × 2); LRMS: m/z = 254 (M^+ – Ac), 237, 222, 205, 177, 145, 135; anal. calcd. for $C_{15}H_{20}O_6$: C 60.80, H 6.80%; found: C 60.98, H 6.95%.



(7)

Synthesis of 2i

Alcohol **18** was prepared according to the literature procedure.[15] IR (neat): ν = 3356, 1657, 1472, 1255, 1115, 1084 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ = 0.08 (s, 6H), 0.91 (s, 9H), 2.08 (br s, 1H), 4.16 (s, 2H), 4.23 (s, 2H), 5.08 (m, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = −5.5 ($CH_3 \times 2$), 18.3 (C), 25.8 ($CH_3 \times 3$), 64.6 (CH_2), 65.1 (CH_2), 111.1 (CH_2), 147.4 (C); LRMS: m/z = 203 ($M^+ + 1$), 184, 173, 113, 69.

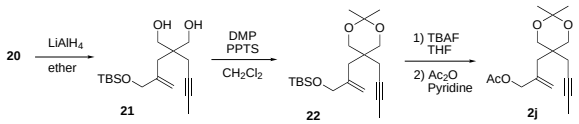
2-(*tert*-Butyldimethylsiloxymethyl)allyl methanesulfonate (19): To a solution of **18** (1.57 g, 7.8 mmol) in CH_2Cl_2 (30 mL) was added triethylamine (Et_3N, 1.6 mL, 11.6 mmol) and methanesulfonyl chloride (MsCl, 0.72 mL, 9.3 mmol) at −10° C and the solution was stirred at the same temperature for 10 min. To this solution was added water, and the aqueous layer was extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The resulting crude product (2.2 g, quant.) was used without further purification. IR (neat): ν = 1654, 1472, 1360, 1254, 1176, 1117, 1085 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ = 0.08 (s, 6H), 0.91 (s, 9H), 3.02 (s, 3H), 4.21 (s, 2H), 4.74 (s, 2H), 5.27 (m, 1H), 5.34 (br s, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = −5.5 ($CH_3 \times 2$), 18.2 (C), 25.8 ($CH_3 \times 3$), 37.8 (CH_3), 63.3 (CH_2), 70.0 (CH_2), 115.8 (CH_2), 141.5 (C); LRMS: m/z = 223 (M^+ – Bu), 153, 129, 113, 79.

Dimethyl 2-[2-(*tert*-butyldimethylsiloxymethyl)allyl]malonate (19a): A crude product which was prepared from **19** (1.1 g, 3.8 mmol), dimethyl malonate (0.86 mL, 7.5 mmol), NaI (530 mg, 3.7 mmol), and NaH (290 mg, 7.5 mmol), according to the procedure for the synthesis of **2f**, was purified by column chromatography on silica gel (hexane/AcOEt, 20:1) to afford **19a** as a colorless oil; yield: 1.1 g (91%). IR (neat): ν = 1740, 1654, 1436, 1254, 1152, 1114, 1082 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ = 0.05 (s, 6H), 0.89 (s, 9H), 2.63 (d, J = 7.8 Hz, 2H), 3.67 (t, J = 7.8 Hz, 1H), 3.71 (s, 6H), 4.07 (s, 2H), 4.84 (m, 1H), 5.06 (m, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = −5.5 ($CH_3 \times 2$), 18.3 (C), 25.8 ($CH_3 \times 3$), 31.7 (CH_2), 50.4 (CH), 52.5 ($CH_3 \times 2$), 65.7 (CH_2), 111.1 (CH_2), 144.7 (C), 169.4 (C × 2); LRMS: m/z = 301 (M^+ – Me), 285, 259, 227, 169, 127; HRMS: m/z calcd. for $C_{15}H_{28}O_5Si$ (M^+): 316.1706; found: 316.1719.

Dimethyl 2-[2-(*tert*-butyldimethylsiloxymethyl)allyl]-2-but-2-ynylmalonate (20): A crude product which was prepared from **19a** (1.1 g, 3.4 mmol), **14** (753 mg, 5.1 mmol), NaI (748 mg, 5.1 mmol), and NaH (174 mg, 4.4 mmol), according to the procedure for the synthesis of **2f**, was purified by column chromatography on silica gel (hexane/AcOEt, 20:1) to afford **20** as a colorless oil; yield: 1.25 g (quant.). IR (neat): ν = 1740, 1654, 1436, 1252, 1206, 1108 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ = 0.05 (s, 6H), 0.91 (s, 9H), 1.76 (t, J = 2.6 Hz, 3H), 2.77 (q, J = 2.6 Hz, 2H), 2.80 (s, 2H), 3.73 (s, 6H), 3.97 (br s, 2H), 4.92 (br, 1H), 5.24 (m, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = −5.4 ($CH_3 \times 2$), 3.4 (CH_3), 18.4 (C), 23.2 (CH_2), 25.9 ($CH_3 \times 3$), 34.5 (CH_2), 52.6 ($CH_3 \times 2$), 57.0 (C), 65.8 (CH_2), 73.6 (C), 79.3 (C), 113.4 (CH_2), 143.1 (C), 170.7 (C × 2); LRMS: m/z = 353 (M^+ – Me), 337 311 251; anal. calcd. for $C_{19}H_{32}O_5Si$: C 61.92, H 8.75%; found: C 62.01, H 8.90%.

Dimethyl 2-but-2-ynyl-2-(2-hydroxymethylallyl)malonate (20a): A crude product which was prepared from **20** (745 mg, 2.0 mmol), and HF (1.0 mL, 48% w/v in water), according to the procedure for the synthesis of **2h**, was used without further purification (**20a:** 660 mg, colorless oil). IR (neat): ν = 3537, 1738, 1648, 1438, 1294, 1294, 1206, 1071 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ = 1.77 (t, J = 2.4 Hz, 3H), 1.93 (br, 1H), 2.79 (q, J = 2.4 Hz, 2H), 2.86 (s, 2H), 3.74 (s, 6H), 3.99 (br, 2H), 4.98 (br, 1H), 5.20 (m, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 3.5 (CH_3), 23.8 (CH_3), 35.1 (CH_2), 52.7 ($CH_3 \times 2$), 57.3 (C), 65.9 (CH_2), 73.4 (C), 79.5 (C), 115.1 (CH_2), 143.9 (C), 170.8 (C × 2).

Dimethyl 2-(2-acetoxymethylallyl)-2-but-2-ynylmalonate (2i): A crude product which was prepared from **20a** (660 mg), pyridine (1.0 mL, 12.0 mmol), and Ac_2O (0.6 mL, 6.0 mmol), according to the procedure for the synthesis of **2g**, was purified by column chromatography on silica gel (hexane/ether, 2:1) to afford **2i** as a colorless oil; yield: 425 mg (72% from **20**). IR (neat): ν = 2236, 1738, 1648, 1240 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ = 1.76 (t, J = 2.6 Hz, 3H), 2.08 (s, 3H), 2.79 (q, J = 2.6 Hz, 2H), 2.88 (s, 2H), 3.73 (s, 6H), 4.42 (s, 2H), 5.08 (br, 1H), 5.21 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 3.5 (CH_3), 20.9 (CH_3), 23.2 (CH_2), 34.9 (CH_2), 52.8 ($CH_3 \times 2$), 57.0 (C), 66.7 (CH_2), 73.3 (C), 79.5 (C), 117.8 (CH_2), 138.5 (C), 170.3 (C), 170.4 (C × 2); LRMS: m/z = 297 ($M^+ + 1$), 266, 237, 177, 117; HRMS: m/z calcd. for $C_{15}H_{20}O_6$ (M^+ – 2 Me): 266.1154; found: 266.1158.



(8)

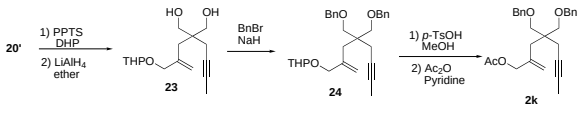
Synthesis of 2j.

2-[2-(*tert*-Butyldimethylsiloxymethyl)allyl]-2-but-2-ynyl-propane-1,3-diol (21): To a suspension of $LiAlH_4$ (148 mg, 4.0 mmol) in ether (2 mL) was added **20** (365 mg, 1.0 mmol) in ether (3 mL) at 0° C, and the solution was stirred at room temperature for 30 min. To this solution was added $Na_2SO_4 \cdot 10\ H_2O$. The solution was stirred for several hours and filtered. The filtrate evaporated. The residue was purified by column chromatography on silica gel (hexane/AcOEt, 2:1) to afford **21** as a colorless oil; yield: 225 mg (72%). IR (neat): $\nu = 3382$, 1648, 1254, 1090 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): $\delta = 0.10$ (s, 6H), 0.92 (s, 9H), 1.80 (t, $J = 2.4$ Hz, 3H), 2.11 (q, $J = 2.4$ Hz, 2H), 2.25 (s, 2H), 3.57 (d, $J = 11.1$ Hz, 2H), 3.62 (d, $J = 11.1$ Hz, 2H), 4.18 (s, 2H), 5.01 (br, 1H), 5.17 (m, 1H).

***tert*-Butyl-[2-(5-but-2-ynyl-2,2-dimethyl[1,3]dioxan-5-yl-methyl)allyloxy]dimethylsilane (22):** To a solution of **21** (350 mg, 1.1 mmol) in CH_2Cl_2 (6 mL) was added DMP (0.3 mL, 2.2 mmol) and PPTS (16 mg) at 0° C and the solution was stirred at room temperature for 15 h. To this solution was added saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography on silica gel (hexane/ether, 10:1) to afford **22** as a colorless oil; yield: 364 mg (92%). ^1H NMR (270 MHz, $CDCl_3$): $\delta = 0.07$ (s, 6H), 0.92 (s, 9H), 1.40 (s, 3H), 1.41 (s, 3H), 1.80 (t, $J = 2.4$ Hz, 3H), 2.08 (s, 1H), 2.33 (q, $J = 2.4$ Hz, 2H), 3.65 (s, 4H), 4.06 (s, 2H), 4.93 (br, 1H), 5.26 (m, 1H).

2-(5-But-2-ynyl-2,2-dimethyl[1,3]dioxan-5-ylmethyl)allyl acetate (2j): To a solution of **22** (360 mg, 1 mmol) in THF (5 mL) was added tetrabutylammonium fluoride (TBAF, 1.0 M in THF, 1.5 mL) at 0° C, and the solution was stirred at room temperature for 1 h. To this solution was added saturated aqueous NH_4Cl and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The residue (240 mg) was used without further purification.

A crude product which was prepared from the above residue (240 mg), pyridine (0.4 ml, 5 mmol) and Ac_2O (0.24 mL, 2.5 mmol), according to the procedure for the synthesis of **2g**, was purified by column chromatography on silica gel (hexane/ether, 5:1) to afford **2j** as a colorless oil; yield: 270 mg (96% from **22**). IR (film): $\nu = 1744$, 1648, 1228, 1196 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.40$ (s, 3H), 1.41 (s, 3H), 1.79 (t, $J = 2.4$ Hz, 3H), 2.10 (s, 3H), 2.21 (s, 2H), 2.28 (q, $J = 2.4$ Hz, 2H), 3.65 (s, 4H), 4.53 (s, 2H), 5.05 (s, 1H), 5.21 (m, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 3.5$ (CH_3), 20.9 (CH_3), 21.7 (CH_2), 22.9 (CH_3), 24.7 (CH_3), 34.9 (CH_2), 36.1 (C), 66.9 ($CH_2 \times 2$), 67.5 (CH_2), 74.9 (C), 78.8 (C), 98.1 (C), 116.5 (CH_2), 139.5 (C), 170.5 (C); LRMS: $m/z = 280$ (M^+), 265, 163; HRMS: m/z calcd. for $C_{16}H_{24}O_4$ (M^+): 280.1674; found: 280.1686.



(9)

Synthesis of 2k.

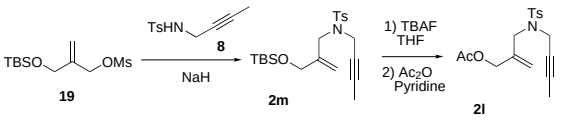
2-But-2-ynyl-2-[2-(tetrahydropyran-2-yloxymethyl)allyl]-propane-1,3-diol (23): A crude product which was prepared from **20a** (603 mg, crude), DHP (0.6 mL, 6.0 mmol), and cat. PPTS (30 mg), according to the procedure for the synthesis of **22**, was used without further purification. (**23a**, 780 mg)

A crude product which was prepared from **23a** (780 mg), $LiAlH_4$ (298 mg, 2 mmol), according to the procedure for the synthesis of **21**, was purified by column chromatography on silica gel (hexane/AcOEt, 1:1) to afford **23** as a colorless oil; yield: 540 mg (96% from **20**). ^1H NMR (270 MHz, $CDCl_3$): $\delta =$ 1.56 – 1.87 (m, 6H), 1.80 (t, $J = 2.4$ Hz, 3H), 2.12 (q, $J = 2.4$ Hz, 2H), 2.25 (d, $J = 14.0$ Hz, 1H), 2.32 (d, $J = 14.0$ Hz, 1H), 2.73 (br, 2H), 3.44 – 3.64 (m, 1H), 3.59 (s, 4H), 3.84 – 3.92 (m, 1H), 3.99 (d, $J = 12.4$ Hz, 1H), 4.28 (d, $J = 12.4$ Hz, 1H), 4.63 (m, 1H), 5.11 (s, 1H), 5.25 (m, 1H).

2-(4,4-Dibenzyloxymethyl-2-methyleneoct-6-ynyloxy)-tetrahydropyran (24): To a suspension of NaH (257 mg, 6.0 mmol) in DMF (4 mL) was added **23** (540 mg, 1.9 mmol) in DMF (6 mL) at 0° C, and the solution was stirred at 0° C for 30 min. To this solution was added benzyl bromide (0.7 mL, 6.0 mmol). The whole solution was stirred at 40° C for 24 h. To this solution was added saturated aqueous NH_4Cl and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography on silica gel (hexane/AcOEt, 19:1) to afford **24** as a colorless oil; yield: 738 mg (84%). ^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.48 - 1.88$ (m, 6H), 1.76 (t, $J = 2.4$ Hz, 3H), 2.20 (s, 2H), 2.24 (q, $J = 2.4$ Hz, 2H), 3.33 - 3.41 (m, 4H), 3.40 – 3.49 (m, 1H), 3.81 – 3.89 (m, 1H), 3.89 (d, $J = 13.5$ Hz, 1H), 4.15 (d, $J = 13.5$ Hz, 1H), 4.49 (s, 4H), 4.59 (t, $J = 3.2$ Hz, 1H), 5.09 (s, 1H), 5.24 (m, 1H), 7.23 – 7.32 (m, 10H).

4,4-Dibenzyloxymethyl-2-methyleneoct-6-yn-1-ol (24a): To a solution of **24** (237 mg, 0.5 mmol) in MeOH (2 mL) was added cat. *p*-TsOH (4.2 mg) at 0° C and the solution was stirred at room temperature for 3 h. To this solution was added saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate, 9:1) to yield **24a** as a colorless oil; yield: 181 mg (94%). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.76$ (t, $J = 1.6$ Hz, 3H), 2.21 – 2.23 (m, 4H), 2.32 (t, $J = 4.3$ Hz, 1H), 3.34 (d, $J = 5.9$ Hz, 2H), 3.39 (d, $J = 5.9$ Hz, 2H), 4.04 (d, $J = 4.3$ Hz, 2H), 4.49 (s, 4H), 4.97 (s, 1H), 5.13 (br, 1H), 7.23 – 7.32 (m, 10H).

4,4-Dibenzyloxymethyl-2-methyleneoct-6-ynyl acetate (2k): A crude product which was prepared from **24a** (580 mg, 1.5 mmol), pyridine (0.7 mL, 9.2 mmol), and Ac_2O (0.4 mL, 4.5 mmol), according to the procedure for the synthesis of **2g**, was purified by column chromatography on silica gel (hexane/AcOEt, 9:1) to afford **2k** as a colorless oil; yield: 606 g (94%). IR (neat): $\nu = 1742$, 1648, 1603, 1228, 1098 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.75$ (t, $J = 2.4$ Hz, 3H), 2.05 (s, 3H), 2.20 (s, 2H), 2.22 (q, $J = 2.4$ Hz, 2H), 3.34 (d, $J = 8.8$ Hz, 2H), 3.38 (d, $J = 8.8$ Hz, 2H), 4.49 (s, 4H), 4.51 (s, 2H), 5.04 (s, 1H), 5.14 (m, 1H), 7.24 – 7.32 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 3.6$ (CH_3), 21.0 (CH_3), 22.7 (CH_2), 33.9 (CH_2), 42.9 (C), 67.6 (CH_2), 71.5 (CH_2), 73.1 (CH_2), 75.6 (C), 77.9 (C), 115.6 (CH_2), 127.2 ($CH \times 2$), 127.3 ($CH \times 2$), 128.1 (CH), 138.6 (C), 140.0 (C), 170.5 (C); LRMS: $m/z = 420$ (M^+), 329, 269, 225, 91; HRMS: m/z calcd. for $C_{27}H_{32}O_4$ (M^+): 420.2300; found: 420.2279.



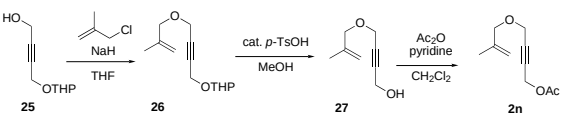
(10)

Synthesis of 2l and 2m

***N*-[2-(*tert*-Butyldimethylsiloxymethyl)allyl]-*N*-but-2-ynyl-4-methylbenzenesulfonamide (2m):** A crude product which was prepared from **8** (980 mg, 4.4 mmol), **19** (1.17 g, 4.1 mmol), NaI (622 mg, 4.2 mmol), and NaH (182 mg, 4.6 mmol), according to the procedure for the synthesis of **2b**, was purified by column chromatography on silica gel (hexane/ether, 7:1) to afford **2m** as a colorless solid; yield: 1.2 g (71%). IR (film): $\nu = 1654, 1597, 1471, 1349, 1162, 1094\ cm^{-1}$; ^1H NMR (270 MHz, $CDCl_3$): $\delta =$ 0.07 (s, 6H), 0.91 (s, 9H), 1.51 (t, $J = 2.4$ Hz, 3H), 2.43 (s, 3H), 3.77 (s, 2H), 4.00 (q, $J = 2.4$ Hz, 2H), 4.13 (s, 2H), 5.10 (s, 1H), 5.29 (s, 1H) 7.29 (d, $J = 8.1$ Hz, 2H), 7.75 (d, $J = 8.1$ Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = -5.4$ ($CH_3 \times 2$), 3.2 (CH_3), 18.3 (C), 21.5 (CH_3), 25.9 ($CH_3 \times 3$), 36.2 (CH_2), 48.7 (CH_2), 63.6 (CH_2), 71.5 (C), 81.7 (C), 113.8 (CH_2), 128.0 (CH x 2), 129.2 (CH × 2), 136.1 (C), 142.4 (C), 143.2 (C); LRMS: $m/z =$ 407 (M^+), 392, 350, 155, 129, 91; HRMS: m/z calcd. for $C_{21}H_{33}NO_3SiS$ (M^+): 407.1950; found: 407.1951.

***N*-But-2-ynyl-*N*-(2-hydroxymethylallyl)-4-methylbenzenesulfonamide (2m'):** To a solution of **2m** (406 mg 1.0 mmol) in THF (5 mL) was added TBAF (1.0 M in THF, 1.5 mL) at 0° C, and the solution was stirred at room temperature for 30 min. To this solution was added saturated aqueous NH_4Cl and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The resulting crude product **2m'** (287 mg) was used without further purification. IR (neat): $\nu = 3536, 2222, 1654, 1346, 1160, 906\ cm^{-1}$; ^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.55$ (t, $J = 2.4$ Hz, 3H), 2.43 (s, 3H), 3.82 (s, 2H), 4.01 (q, $J = 2.4$ Hz, 2H), 4.17 (s, 2H), 5.09 (s, 1H), 5.21 (s, 1H) 7.31 (d, $J = 8.3$ Hz, 2H), 7.76 (d, $J = 8.3$ Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 3.2$ (CH_3), 21.5 (CH_3), 36.3 (CH_2), 48.5 (CH_2), 63.3 (CH_2), 71.4 (C), 81.8 (C), 115.5 (CH_2), 127.9 (CH × 2), 129.3 (CH × 2), 135.8 (C), 142.8 (C), 143.5 (C).

2-{[But-2-ynyl-(4-toluenesulfonyl)amino]methyl}allyl acetate (2l): A crude product which was prepared from **2m'** (287 mg), pyridine (0.2 mL, 2 mmol), and Ac_2O (0.14 mL, 1.5 mmol), according to the procedure for the synthesis of **2g**, was purified by column chromatography on silica gel (hexane/ethyl acetate, 5:1) to afford **2l** as a colorless solid; yield: 298 mg (91% from **2m**). IR (film): $\nu = 1654, 1597, 1471, 1349, 1162, 1094\ cm^{-1}$; ^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.52$ (t, $J = 2.4$ Hz, 3H), 2.10 (s, 3H), 2.43 (s, 3H), 3.82 (s, 2H), 4.00 (q, $J = 2.4$ Hz, 2H), 4.59 (s, 2H), 5.23 (s, 1H), 5.25 (s, 1H) 7.30 (d, $J = 8.3$ Hz, 2H), 7.74 (d, $J = 8.3$ Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 3.2$ (CH_3), 20.9 (CH_3), 21.5 (CH_3), 36.3 (CH_2), 48.8 (CH_2), 64.3 (CH_2), 71.3 (C), 81.8 (C), 117.4 (CH_2), 127.8 (CH × 2), 129.2 (CH × 2), 135.8 (C), 137.9 (C), 143.3 (C), 170.4 (C); LRMS: $m/z = 276$ ($M^+ - AcO$), 180, 155, 138, 120, 91; HRMS: m/z calcd. for $C_{15}H_{18}NO_2S$ ($M^+ - AcO$): 276.1058; found: 276.1044.



(11)

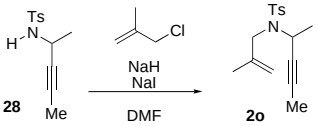
Synthesis of 2n

Alcohol **25** was prepared according to the literature procedure.[16]

2-[4-(2-Methylallyloxy)-but-2-ynyloxy]tetrahydropyran (26): A crude product which was prepared from **25** (520 mg, 3.0 mmol), methallyl chloride (0.5 ml, 5 mmol), NaI (320 mg, 2.1 mmol), and NaH (200 mg, 5 mmol), according to the procedure for the synthesis of **24**, was purified by column chromatography on silica gel (hexane/ether, 5:1) to afford **26** as a colorless oil; yield: 670 mg. ^1H NMR (270 MHz, $CDCl_3$): $\delta =$ 1.51 – 1.85 (m, 6H), 1.74 (s, 3H), 3.49 – 3.56 (m, 1H), 3.79 – 3.88 (m, 1H), 3.96 (s, 2H), 4.16 – 4.18 (m, 2H), 4.22 – 4.39 (m, 2H), 4.81 (t, $J = 3.2$ Hz, 1H), 4.91 (s, 1H), 4.97 (m, 1H).

4-(2-Methylallyloxy)-but-2-yn-1-ol (27): A crude product which was prepared from **26** (670 mg, 3 mmol), cat. *p*-TsOH (19 mg), according to the procedure for the synthesis of **24a**, was purified by column chromatography on silica gel (hexane/ether, 2:1) to afford **27** as a colorless oil; yield: 390 mg (93% from **26**). IR (neat): $\nu = 3395, 1654, 1449, 1352, 1124, 1078, 1017, 903\ cm^{-1}$; ^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.72$ (s, 3H), 2.36 (br, 1H), 3.94 (s, 2H), 4.15 (d, $J = 1.9$ Hz, 2H), 4.29 (d, $J =$ 1.9 Hz, 2H), 4.90 (s, 1H), 4.96 (s, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 19.4$ (CH_3), 50.8 (CH_2), 57.1 (CH_2), 73.6 (CH_2), 81.5 (C), 84.6 (C), 113.0 (CH_2), 141.2 (C).

4-(2-Methylallyloxy)but-2-ynyl acetate (2n). A crude product which was prepared from **27** (390 mg, 2.8 mmol), pyridine (1.0 mL, 12 mmol), and Ac_2O (0.5 mL, 5 mmol), according to the procedure for the synthesis of **2g**, was purified by column chromatography on silica gel (hexane/AcOEt, 9:1) to afford **2n** as a colorless oil; yield: 460 mg (91%); IR (neat): $\nu = 1749, 1654, 1377, 1357, 1224, 1136, 1082, 1028\ cm^{-1}$; ^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.75$ (s, 3H), 2.10 (s, 3H), 3.96 (s, 2H), 4.17 (m, 2H), 4.72 (m, 2H), 4.93 (br, 1H), 4.99 (br, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 19.4$ (CH_3), 20.6 (CH_3), 52.2 (CH_2), 57.1 (CH_2), 73.7 (CH_2), 80.1 (C), 82.8 (C), 113.0 (CH_2), 141.3 (C), 170.1 (C); LRMS: $m/z = 125, 111, 97, 79$.



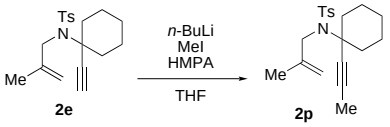
(12)

Synthesis of 2o

Sulfonamide **28** was prepared according to the literature procedure.[12]

4-Methyl-*N*-(2-methylallyl)-*N*-(1-methylbut-2-ynyl)benzenesulfonamide (2o): A crude product which was prepared from **28** (711 mg, 3.0 mmol), methallyl chloride (0.44 mL, 4.5 mmol), NaI (666 mg, 4.5 mmol), and NaH (150 mg, 3.6 mmol), according to the procedure for the synthesis of **2b**, was purified by column chromatography on silica gel (hexane/AcOEt, 5:1) to afford **2o** as a colorless oil; yield: 855 mg (98%). IR (neat): $\nu = 2240, 1659\ 1596, 1494, 1451, 1338, 1160, 1106\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.36$ (d, $J =$ 6.8 Hz, 3H), 1.55 (d, $J = 2.4$ Hz, 3H), 1.81 (s, 3H), 2.42 (s, 3H), 3.61 (d, $J = 16.4$ Hz, 1H), 3.82 (d, $J = 16.4$ Hz, 1H), 4.79 – 4.84 (m, 1H), 4.89 (s, 1H), 5.03 (s, 1H), 7.28 (d, $J = 8.4$ Hz, 2H), 7.72 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 3.1$

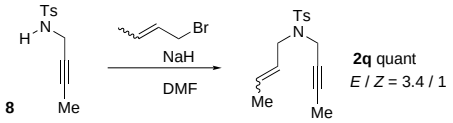
(CH_3), 20.0 (CH_3), 21.4 (CH_3), 22.5 (CH_3), 47.1 (CH), 50.7 (CH_2), 76.3 (C), 81.1 (C), 112.8 (CH_2), 127.7 (CH × 2), 129.2 (CH × 2), 136.2 (C), 142.7 (C), 143.0 (C); LRMS: *m/z* = 276 (M^+ – Me), 198, 155, 120, 108, 91; HRMS: *m/z* calcd. for $C_{15}H_{19}NO_2S$ (M^+): 291.1293; found: 291.1284.



(13)

Synthesis of 2p

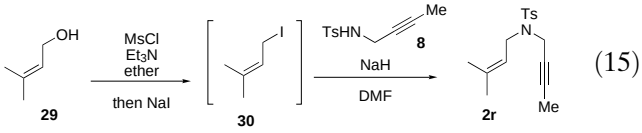
4-Methyl-*N*-(2-methylallyl)-*N*-(1-prop-1-ynylcyclohexyl)benzenesulfonamide (2p): To a solution of **2e** (675 mg, 2.0 mmol) in THF (4 mL) was added *n*-BuLi (1.3 mL, 2.1 mmol, 1.66 M in hexane) at −78° C, and the solution was stirred at −78° C for 30 min. To this solution was added MeI (0.15 mL, 2.5 mmol) and HMPA (0.7 mL, 4.1 mmol) and the whole solution was warmed to room temperature for 4 h. To this solution was added water, and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography on silica gel (hexane/AcOEt, 9:1) to afford **2p** as colorless crystals; yield: 690 mg (98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07 – 1.62 (m, 6H), 1.59 (s, 3H), 1.80 (s, 3H), 1.84 (dt, *J* = 2.4, 8.4 Hz, 2H), 2.00 (d, *J* = 7.6 Hz, 2H), 2.41 (s, 3H), 4.07 (s, 2H), 4.93 (m, 1H), 5.12 (br, 1H), 7.26 (d, *J* = 8.2 Hz, 2H), 7.71 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 3.4 (CH_3), 20.3 (CH_3), 21.5 (CH_3), 23.5 (CH_2 × 2), 24.7 (CH_2), 37.7 (CH_2 × 2), 53.5 (CH_2), 62.4 (C), 74.9 (CH), 83.2 (C), 111.9 (CH_2), 127.5 (CH × 2), 129.2 (CH × 2), 139.5 (C), 142.9 (C), 143.3 (C); LRMS: *m/z* = 345 (M^+), 330, 316, 289, 274, 190, 155, 120, 91; HRMS: *m/z* calcd. for $C_{20}H_{27}NO_2S$ (M^+): 345.1762; found: 345.1760.



(14)

Synthesis of 2q

***N*-But-2-enyl-*N*-but-2-ynyl-4-methylbenzenesulfonamide (2q):** A crude product which was prepared from **8** (667 mg, 3.0 mmol), crotyl bromide (0.45 mL, 3.6 mmol), and NaH (153 mg, 3.6 mmol), according to the procedure for the synthesis of **2b**, was purified by column chromatography on silica gel (hexane/AcOEt, 5:1) to afford **2q** as colorless crystals; yield: 828 mg (99%). Spectral data for *(E)*-**2q**: mp (ether/hexane) 49.0 – 50.5° C; IR (nujol): ν = 2217, 1670, 1597, 1347, 1164 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.54 (t, *J* = 2.4 Hz, 3H), 1.68 (dd, *J* = 6.8, 1.6 Hz, 3H), 2.42 (s, 3H), 3.72 (d, *J* = 6.8 Hz, 2H), 4.00 (q, *J* = 2.4 Hz, 2H), 5.32 – 5.40 (m, 1H), 5.64 – 5.73 (m, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 3.2 (CH_3), 17.6 (CH_3), 21.4 (CH_3), 36.0 (CH_3), 48.2 (CH_2), 71.8 (C), 81.3 (C), 124.8 (CH), 127.9 (CH × 2), 129.1 (CH × 2), 131.1 (CH), 136.4 (C), 143.1 (C); LRMS: *m/z* = 277 (M^+), 262, 236, 222, 212, 198, 184, 155, 139, 122, 91; anal. calcd. for $C_{15}H_{19}NO_2S$: C 64.95, H 6.90, N 5.05 S 11.56%; found: C 65.01, H 7.03, N 5.02, S 11.44%.

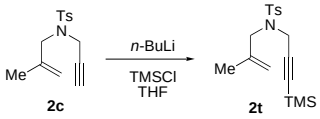


(15)

Synthesis of 2r

***N*-But-2-ynyl-4-methyl-*N*-(3-methylbut-2-enyl)benzenesulfonamide (2r):** To a solution of **29** (0.6 mL, 6.0 mmol) in ether (10 mL) was added Et_3N (1.3 mL, 9.0 mmol), and MsCl (0.5 mL, 6.0 mmol) at −78° C and the solution was warmed to 0° C for 2 h. To this solution was added NaI (1.0 g, 6.6 mmol) at 0° C and the solution was stirred at the same temperature for 20 min. The resulting solution (**30** in ether) was used without further purification.

A crude product which was prepared from **8** (990 mg, 4.4 mmol), **30** in ether (*ca.* 6.0 mmol), and NaH (239 mg, 6.0 mmol), according to the procedure for the synthesis of **2b**, was purified by column chromatography on silica gel (hexane/AcOEt, 9:1) to afford **2r** as colorless crystals; yield: 1.3 g (99%); mp (ether/hexane) 59.0 – 60.0° C; IR (nujol): ν = 2208, 1675, 1596, 1344, 1158 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.53 (t, *J* = 2.4 Hz, 3H), 1.66 (s, 3H), 1.72 (s, 3H), 2.43 (s, 3H), 3.77 (d, *J* = 7.6 Hz, 2H), 3.99 (q, *J* = 2.4 Hz, 2H), 5.10 (m, 1H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.74 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 3.0 (CH_3), 17.6 (CH_3), 21.3 (CH_3), 25.6 (CH_3), 35.8 (CH_2), 43.7 (CH_2), 71.8 (C), 81.1 (C), 118.0 (CH), 127.7 (CH × 2), 129.0 (CH × 2), 136.0 (C), 138.4 (C), 142.9 (C); LRMS: *m/z* = 291 (M^+), 276, 262, 236, 222, 184, 155, 136, 120, 107, 91; anal. calcd. for $C_{16}H_{21}NO_2S$: C 65.95, H 7.26, N 4.81, S 11.00%; found: C 65.96, H 7.40, N 4.89, S 11.00%.



(16)

Synthesis of 2t

4-Methyl-*N*-(2-methylallyl)-*N*-[3-(trimethylsilyl)prop-2-ynyl]benzenesulfonamide (2t): A crude product which was prepared from **2c** (1.0 g, 3.9 mmol), *n*-BuLi (3.3 mL, 5.0 mmol, 1.5 M in hexane), and TMSCl (1.0 mL, 8.0 mmol), according to the procedure for the synthesis of **2p**, was purified by column chromatography on silica gel (hexane/AcOEt, 15:1) to afford **2t** as colorless crystals; yield: 800 mg (62%); mp (ether/hexane) 84 – 85.5° C; IR (nujol): ν = 2175, 1654, 1599, 1344, 1166 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = −0.02 (s, 9H), 1.78 (s, 3H), 2.42 (s, 3H), 3.73 (s, 2H), 4.06 (s, 2H), 4.96 (m, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.74 (d, *J* = 8.1Hz, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = −0.4 (CH_3 × 3), 19.7 (CH_3), 21.5 (CH_3), 36.5 (CH_2), 52.3 (CH_2), 90.9 (C), 97.7 (C), 115.5 (CH_2), 127.8 (CH × 2),

129.5 (CH × 2), 136.1 (C), 139.1 (C), 143.3 (C); LRMS: m/z = 335 (M^+), 320, 294, 180, 155, 91; anal. calcd. for $C_{17}H_{25}NO_2SSi$: C 60.85, H 7.51, N 4.17, S 9.56%; found: C 60.85, H 7.49, N 4.09, S 9.75%.

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[6] In the synthesis of an eight-membered ring compound using ruthenium catalyst **1a**, we considered two similar possibilities (formation of eight- or nine-membered ring compounds), but only an eight-membered ring compound was formed.[2h]

[7] In most cases, it is difficult to isolate five- and six-membered ring compounds. In some cases, after performing column or flash chromatography on silica gel several times, each pure compound could be isolated. Based on the ^{1}H NMR spectra of the isolated five- and six-membered ring compounds, we could determine their ratio. That is, the ring protons at the 2 and 5 positions

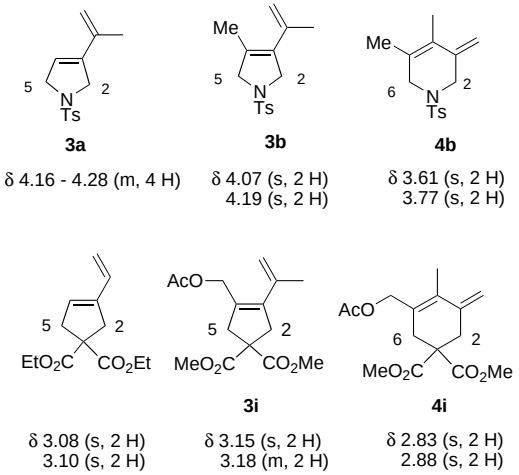

Figure 2.

appeared at lower fields than those at the 2 and 6 positions of six-membered ring compounds (Figure 2). The ratio of the five- to six-membered ring compounds was determined on the basis of these results.

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