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Rhodium-Catalyzed [4+2+2] Cycloaddition Reaction of Two Enynes or Diynes with One Diene to Give Eight-Membered Ring Compounds

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Abstract: A new $[Rh(cod)Cl]_2$/AgX (cod=1,5-cyclooctadiene)-catalyzed intermolecular [4+2+2] cycloaddition reaction between two enynes with one diene, and between two diynes and one diene has been developed. This is the first example of a rhodium-catalyzed trimolecular and three-component [4+2+2] cycloaddition to form eight-membered ring compounds. The yield of the reaction was highly dependent upon the counteranion and the reaction medium. The best yields were obtained when the reaction was carried out in toluene with OTf^- anions. The regioselectivity was highly dependent upon the substrates. Relatively high regioselectivities were obtained for the cycloaddition of two enynes with one diene. In some cases, only one regioisomer was obtained. However, the regioselectivities for the cycloaddition of two diynes with one diene were rather poor. The use of a syringe pump in the slow addition of reactants slightly enhanced the regioselectivity.

Keywords: alkynes; [4+2+2] cycloaddition; dienes; homogeneous catalysis; 8-membered rings; rhodium

Introduction

Metal-catalyzed cycloadditions are of great relevance in modern organic synthesis since they usually provide prominent methods for the construction of cyclic frameworks in structurally and functionally complex molecules at a relatively low economical and ecological cost.[1] For this reason, developing new types of cycloadditions that allow the transformation of readily available substrates into target-relevant products using the metal catalyst is a highly challenging task.[2] Although a number of assembly modes has been documented for the construction of three- to seven-membered carbocycles, higher-order cycloadditions are less common because cyclization strategies are often regarded as inappropriate due to entropic factors that impede ring closure. However, unsaturated compounds can be brought together and activated on a transition metal that acts as a template. Thus, the use of a transition metal has made feasible cycloaddition reactions that are otherwise difficult or impossible.

The development of new strategies for the efficient construction of eight-membered rings from readily available starting materials continues to be important for accessing natural products and their structural variants,[3] as well as for generating novel scaffolds towards application in chemical biology and pharmaceutical research.[4] Recently, a handful of transition metal-catalyzed [4+4], [6+2], and [4+2+2] cycloaddition reactions has been reported.[5] We expected that the [4+2+2] cycloaddition reactions would provide an eight-membered ring with a greater variety of functional groups than any other method. The reported [4+2+2] cycloaddition reactions look like trimolecular and three-component cycloadditions. However, the known transition metal-catalyzed [4+2+2] reactions are bimolecular and three-component cycloadditions of enynes with 1,3-butadiene, diynes with alkynes, diynes with 1,3-butadienes, diene-enes with alkynes, or dienynes to dimers. Although there have been many reports on trimolecular cycloadditions, such as [5+2+1],[6] [2+2+2],[7] and, [4+4+1][8] cycloadditions, trimolecular [4+2+2] cycloadditions catalyzed by transition metals have not been forthcoming. Very recently, a three-molecular [3+2+2] cycloaddition of ethyl cyclopropylideneacetate and alkynes has been reported.[9] We envisioned that this type of carbocyclization would afford mixtures of regioisomers. However, if we circumvent the problems

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associated with poor regioselectivity, then these reactions would facilitate a rapid increase in molecular diversity and complexity.

While we were studying a cycloaddition reaction of enynes with butadiene catalyzed by $[Rh(cod)Cl]_2$/AgX (cod = 1,5-cyclooctadiene), we observed the formation of eight-membered ring compounds from a reaction of butadiene (4π) with two triple bonds (2× 2π) from two enynes. The reaction was an example of a trimolecular and three-component cycloaddition. Moreover, this [4+2+2] trimolecular and three-component cycloaddition can be extended to the cycloaddition reaction between two diynes and one diene. Diynes are highly appealing substrates in the [4+2+2] cycloaddition, but their use is restricted to a formal ruthenium-catalyzed [4+2+2] cycloaddition of 1,6-diynes to 1,3-dienes.[5i] We herein report the rhodium-catalyzed [4+2+2] cycloaddition between two enynes and one diene, and between two diynes and one diene, resulting in the synthesis of eight-membered rings. This is the first example of a rhodium-catalyzed, trimolecular and three-component [4+2+2] cycloaddition to afford eight-membered ring compounds. There were some examples of a tandem reaction that looked like a trimolecular and three-component [4+2+2] cycloaddition reaction.[5h]

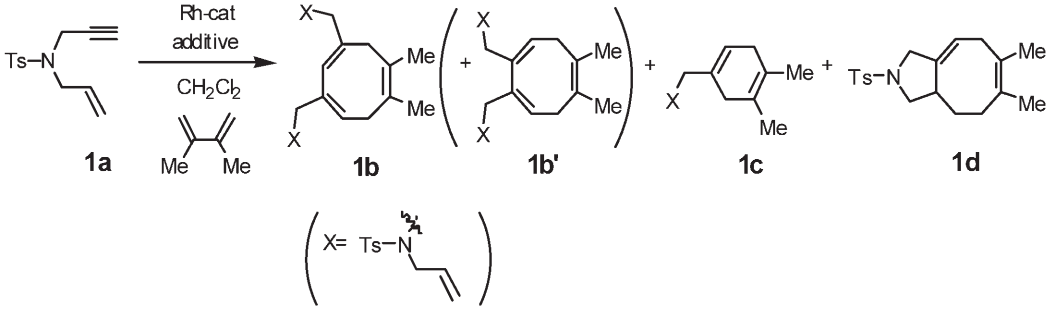
Results and Discussion

[4+2+2] Cycloaddition between Two Enynes (or Diynes) with One Diene

Using an enyne (**1a**) having N-Ts as a tether, we studied the rhodium-catalyzed cycloaddition reaction (Table 1).

When **1a** was treated with $[Rh(cod)Cl]_2$, for 4 days (entry 1) until all the reactant had disappeared, a mixture of **1b**, **1b′**, **1c**, and **1d** was obtained in the ratio of 24:6:43:10. Compounds **1b** and **1b′** were newly discovered eight-membered ring compounds, **1c** was similar to the compounds reported by Evans, and **1d** was a Diels–Alder reaction product. The formation of **1b** and **1b′** was quite different from the results obtained by the Evans and Gilbertson groups.[5h,i] They also reported quite similar reactions, but did not observe the formation of compounds derived from a similar trimolecular and three-component cycloaddition. We screened reaction conditions to explore the possibility

Table 1. Rh(I)-catalyzed intermolecular cycloaddition of enyne **1a** with the diene.



Entry[a]	Additive	Solvent	Time	Temperature [°C]	Yield [%][b]		
					(1b+1b′)	**1c**	**1d**
1	none	CH_2Cl_2	4 day	r.t.	30(4/1)	43	10
2	$AgBF_4$	CH_2Cl_2	10 min	r.t.	34(4/1)	25	38
3	$AgSbF_6$	CH_2Cl_2	30 min	r.t.	30(6/1)	20	50
4	$AgClO_4$	CH_2Cl_2	30 min	r.t.	77(7/1)	11	10
5	AgOTf	CH_2Cl_2	30 min	r.t.	81(5/1)	15	-
6	AgOTf	CH_3CN	24 h	r.t.	n.r.[c]	-	-
7	AgOTf	THF	3 h	r.t.	90(3/1)	8	-
8	AgOTf	Toluene	3 h	r.t.	95(2/1)	-	-
9[d]	AgOTf	Toluene	3 h	r.t.	80(2/1)	10	-
10	AgOTf	Toluene	1 h	70	80(3/1)	-	9
11[e]	AgOTf	Toluene	3 h	r.t.	85(8/1)	-	-

[a] 2 equivs. AgX (per Rh) were used.
[b] Isolated yield.
[c] No reaction.
[d] Enyne was added in advance.
[e] Syringe pump was used.

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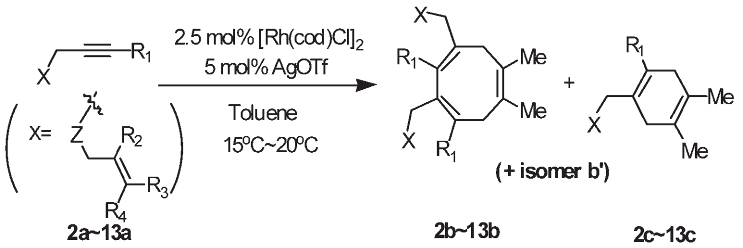
Table 2. Rh(I)-catalyzed intermolecular [4+2+2] or [4+2] cycloaddition.



Entry[a]	Enyne	tether(Z)	R_1	R_2	R_3	R_4	Time	Ratio (**b**/**b′**)	Yield [%][b] (**b**+**b′**)/(**c**)
1	**2a**	NMts[c]	H	H	H	H	2 h	8.2/1	94 (94/0)
2	**3a**	NNaph[d]	H	H	H	H	2 h	3.8/1	87 (87/0)
3	**4a**	$C(CH_2OR)_2$[e]	H	H	H	H	5 h	(**b** only)	41 (41/0)
4	**5a**	$C(CO_2Et)_2$	H	H	H	H	5 days	(**b** only)	3 (3/0)[f]
5	**6a**	$C(SO_2Ph)_2$	H	H	H	H	5 days	N.A	n.r.[g]
6	**7a**	NTs	Me	H	H	H	7 h	(**b** only)	20(20/0)
7	**8a**	NTs	H	Me	H	H	2 h	(**b** only)	98(75/23)
8	**9a**	NTs	H	H	Me	H	1 h	(**b** only)	98(98/0)
9	**10a**	NTs	H	H	Me	Me	5 h	(8/1)	83(35/48)
10	**11a**	NTs	H	H	Ph	H	2 h	(**b** only)	97(95/2)
11	**12a**	NNaph	H	H	Ph	H	2 h	(**b** only)	95(90/5)
12	**13a**	O	H	H	Ph	H	5 h	(**b** only)	92(82/10)

[a] 0.8 mmol enyne, 2.5 mol% $[Rh(cod)Cl]_2$, 5 mol% AgOTf, and 1.5 equivs. 2,3-dimethylbutadiene were used in 3 mL toluene.

[b] Isolated yield.

[c] NMts = 3,5-dimethylbenzenesulfonamide.

[d] NNaph = naphthalenesulfonamide.

[e] $R = (C(CH_3)_2)$.

[f] 95% reactant was recovered.

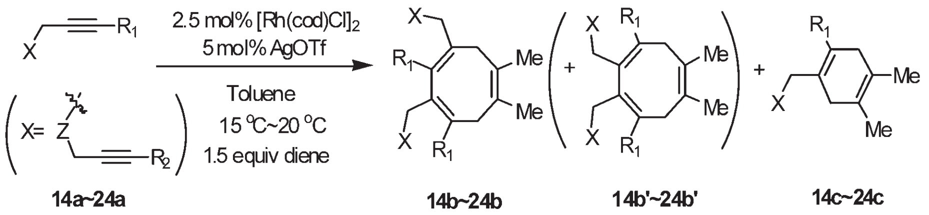
[g] No reaction.

of exclusive formation of **1b** or **1b′**. As shown in Table 1, cationic Rh(I) catalysts (entries 2–11) were found to be superior to the neutral Rh(I) catalyst (entry 1) for facilitating cycloaddition. The remarkable catalytic efficiency of this process is highlighted by its mild reaction conditions and short reaction time. Evans et al.[5h] carried out the catalytic reaction using $RhCl(PPh_3)_3$/AgOTf in refluxing toluene for 12 h. Gilbertson et al.[5i] conducted the catalytic reaction using $[Rh(NBD)Cl]_2$/$AgSbF_6$/Me-DuPHOS in the mixed solvent CH_2Cl_2 and EtOAc (6:1) at 60°C for 12 h. The combined yield of **1b** and **1b′** and the ratio of **1b**:**1b′** were highly dependent upon the counteranion (entries 2–5) and the reaction medium (entries 5–8). Interestingly, when acetonitrile was used as a solvent (entry 6), no reaction was observed. The best combined yield (95%) was obtained when the reaction was carried out in the presence of AgOTf as an additive in toluene solution for 3 h (entry 8). However, the regioisomer ratio (2:1) was rather poor. When the addition sequence of **1a** and 2,3-dimethyl-1,3-butadiene was reversed under the same reaction conditions (entry 9), the yield of **1b** and **1b′** decreased slightly to 80% and formation of **1c** was observed. When the reaction temperature was increased to 70°C (entry 10), the yield of **1b** and **1b′** was decreased to 80%, the ratio **1b**:**1b′** was 3:1, and **1d** was isolated in 9% yield. Interestingly, when the reactant was added at room temperature for 1 h using a syringe pump and the resulting solution was stirred for 2 h (entry 11), the ratio of **1b**:**1b′** was 8:1 with an 85% combined yield. Thus, the regioselectivity observed was acceptable but was not high enough compared to Evans' result.[5h]

With this result in hand, we next examined the generality of the reaction with a range of different enyne substrates with 2,3-dimethyl-1,3-butadiene (Table 2).

Substrates with a nitrogen tether reacted smoothly to give the corresponding products with high yields. However, substrates (entries 3 and 4) with acetal and malonate tethers are inferior to the previous substrates with, respectively, 41% and 3% yield of **4b** and **5b** as the sole product. For a substrate with a phenylsulfonate tether, no corresponding products were observed (entry 5). It is also important to note that in all cases except entries 1, 2, and 9 only **b** was formed. Thus, the process was highly regioselectivie for some enyne substrates. In the cases of entries 1 and 2, the

Table 3. Rh-catalyzed three-component [4+2+2] cycloaddition of diyne with diene.[a]



Entry	Diyne	X			Time	Ratio (**b**:**b'**)	Yield [%][b] (**b**+**b'**)/**c**
		Z	R_1	R_2			
1	**14a**	NTs	H	Ph	3 h	1:2.3	95 (95/0)
2	**15a**	NTs	Ph	Ph	12 h	-	10 (0/10)
3	**16a**	NMts[c]	H	Ph	3 h	1:17	99 (72/17)
4	**17a**	NNaph[d]	H	Ph	3 h	1:2.8	94 (94/0)
5	**18a**	O	H	Ph	3 h	1:4.5	71 (71/0)
6	**19a**	NTs	H	Me	2 h	1:0.9	76 (76/0)
7	**20a**	NTs	H	Et	3 h	1:3.2	81 (67/14)
8	**21a**	NTs	H	*c*-Pr[e]	3 h	1:2.1	65 (62/3)
9	**22a**	NTs	H	cyclohexenyl	5 h	1:1.3	72 (72/0)
10	**23a**	NTs	H	*p*-tolyl	5 h	1:2.1	86 (86/0)
11	**24a**	NTs	H	4-methoxyphenyl	4 h	1:2.2	87 (78/9)

[a] 0.8 mmol of diyne, 2.5 mol% [Rh(cod)Cl]$_2$ (10 mg), and 5 mol% AgOTf (10 mg) were reacted in 3 mL toluene at room temperature.

[b] Isolated yield.

[c] NMts = 3,5-dimethylbenzenesulfonamide.

[d] NNaph = naphthalenesulfonamide.

[e] *c*-Pr = C_3H_5.

use of a syringe pump enhanced the isomer ratio of **b**:**b'** from 6.6:1 to 8.2:1 and 2.8:1 to 3.8:1, respectively. Thus, the use of a syringe pump in the slow addition of reactants slightly enhanced the regioselectivity. When a methyl group was introduced to **1a** (entries 6–9), the combined yield of **b** and **b'** and the reaction time varied greatly: the introduction of the methyl group to an alkyne terminus (R_1) (entry 6) decreased the combined yield of **b** and **b'** to 20% and lengthened the reaction time to 7 h. However, the introduction of the methyl group to an alkene terminus (R_3) (entry 8) led to an increase in the combined yield of **b** and **b'** to 98% and shortened the reaction time to 1 h. When the number of methyl groups increased to two (entry 9), a considerable amount of Diels–Alder product was formed. When R_3 was fixed with a phenyl group (entries 10–12), high yields of **b** (82–95%) were obtained with the concomitant formation of Diels–Alder products (2–10%).

As an extension of the above reaction, we examined a rhodium-catalyzed [4+2+2] cycloaddition reaction of two diynes and one diene (Table 3).

We adopted the reaction conditions from the above study: [Rh(cod)Cl]$_2$ (2.5 mol%), AgOTf (5 mol%), toluene (3 mL), at room temperature, and using a syringe pump. This study demonstrated that nitrogen- and oxygen-containing tethered diynes furnish the corresponding cycloadducts in reasonable to high yields (62–94%). However, the ratio of **b**:**b'** varied significantly depending upon the diyne substrate. In the cycloaddition reaction without using a syringe pump, two eight-membered ring compounds, unsymmetrical **14b** and symmetrical **14b'**, were obtained in 95% yield with a ratio of 40:55 from a diyne (**14a**). Interestingly, the symmetrical isomer was more favored than the unsymmetrical one. This kind of observation was not found in the cycloaddition of enynes with a diene. In the [4+2+2] cycloaddition of two enynes with one diene, unsymmetrical 8-membered compounds were usually obtained as major products. Compounds **14b** and **14b'** were easily separated by chromatography. When the reactant was added using a syringe pump at room temperature for 1 h, the ratio of **14b**:**14b'** was changed to 1:2.3 (entry 1). Thus, slow addition was more favorable to the formation of **14b'** than **14b**. Reaction of an internal diyne (**15a**) with 2,3-dimethylbuta-1,3-diene yielded 10% of a Diels–Alder reaction product (**15c**) with 66% recovery of the starting diyne (entry 2). For an N-Mts-tethered diyne substrate (entry 3), the regioselectivity was quite high (1:17). However, the regioselectivity for an N-Naph-tethered diyne substrate (entry 4) was moderate (1:2.8). A higher regioselectivity (1:4.5) was obtained for an oxygen-tethered substrate (entry 5). For

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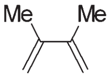
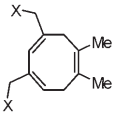
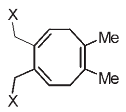
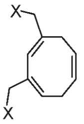
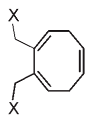
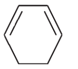
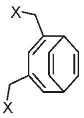
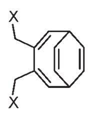
Table 4. Rh(I)-catalyzed intermolecular [4+2+2] cycloaddition with various dienes.

Entry	Diene[a]	Reactant(enyne or diyne)	Product				Time [h]	(**e**/**e′**) (or **b**/**b′**)	Yield [%][b]
1		**1a**		**1b**		**1b′**	3	8:1	85 (76/9)
2		**14a**		**14b**		**14b′**	3	0.43:1	79 (24/55)
3		**1a**		**1e**		**1e′**	3	only 2	33 (33/0)[c]
4		**14a**		**14e**		**14e′**	3	7.3:1	58 (51/7)
5		**1a**		**1f**		**1f′**	2	2.8:1	83 (61/22)
6		**14a**		**14f**		**14f′**	2	5.6:1	33 (28/5)

[a] 0.8 mmol of diyne, 2.5 mol% [Rh(cod)Cl]$_2$ (10 mg), and 5 mol% AgOTf (10 mg) were reacted in 3 mL toluene at room temperature.

[b] Isolated yield.

[c] The concomitant formation of the bimolecular [4+2+2] cycloaddition reaction product in 37% yield was observed.

N-Ts-tethered diynes (entries 6–11), the ratio of **b**:**b′** ranged from 1:0.9 to 1:3.2. For entry 6, the isomer **b′** was slightly more favorable than **b**. Thus, it seemed that the tether atom, and the substituent on the tether atom, had a major influence on the ratio of **b**:**b′**. Interestingly, when the reactants were added by using a syringe pump for 1.5 h, the isomer **b** became more favorable than **b′**. However, the effect of the use of the syringe pump was not great. Overall, relatively poor regioselectivities were observed. In order to enhance the regioselectivity, additives such as PPh$_3$ and BINAP were added. However, the addition of phosphines resulted in an inferior reaction.

We next examined the generality of the reaction with a range of different diene substrates with enyne (**1a**) or diyne (**14a**) (Table 4).

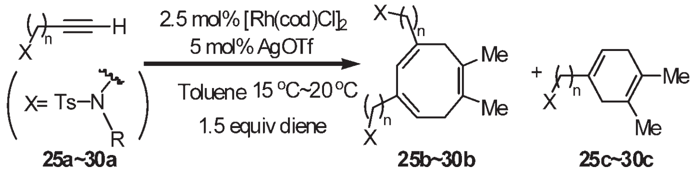
In the reaction of butadiene with **1a** (entry 3), only one regioisomer **1e** was obtained in 33% yield with the concomitant formation of a bimolecular [4+2+2] cycloaddition reaction product **1d′** (37%). In the reaction with **14a** (entry 4), two eight-membered ring compounds, **14e** and **14e′**, were obtained in 58% yield with a ratio of 51:7. Thus, the use of butadiene instead of 2,3-dimethylbutadiene led to relatively moderate to reasonable yields with relatively high regioselectivities. When cyclohexadiene was used as a diene substrate (entry 5), the eight-membered ring products **1f** and **1f′** were obtained in 83% yield, with a ratio of 2.8:1. Treatment of cyclohexadiene with **14a** (entry 6) provided **14f** and **14f′** in 33% yield with a ratio of 28:5. Thus, the use of cyclohexadiene instead of 2,3-dimethylbutadiene gave a relatively lower regioselectivity for **1a** and a better and reversed regioselectivity for **14a**. Overall, the regioselectivity and yield of the [4+2+2] cycloaddition reactions were greatly influenced by the dienes used.

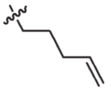
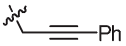
Reaction Mechanisms

It is expected that higher-order reactions often provide only low regioselectivities of adducts because of low periselectivity, which is a consequence of the extended π systems involved and the fact that they frequently participate in multiple competitive pericyclic events. However, to gain insight into the mechanism of the [4+2+2] cycloaddition reaction of two enynes with one diene, we studied the following reactions (Table 5).

When an alkyne substrate **25a** was used instead of enyne substrates, a Diels–Alder reaction product **25c** was obtained as the sole product in 70% yield. Enynes (**26a**, **27a**, **28a**) having tethers lengthened by one or two carbon(s) produced the corresponding [4+2+2] cycloaddition products, **26b**, **27b**, and **28b**, respectively, as major products. These observations suggest that in order to obtain a [4+2+2] cycloaddition product, enyne substrates were necessary although the alkene moiety did not participate in the cycloaddition reaction product. There should be some role of the alkene moiety in the cycloaddition reaction. Treatment of a diyne (**29a**) with a chain lengthened by one carbon in the internal alkyne with 2,3-dimethylbuta-1,3-diene for 12 h gave a Diels–Alder reaction product in 53% yield with 12% recovery of the starting diyne. When a diyne (**30a**) with a chain lengthened by one carbon in the terminal alkyne was reacted with 2,3-dimethylbuta-1,3-diene for 24 h, a Diels–Alder reaction product was obtained in 48% yield, with 37% recovery of the starting diyne. Thus, the chain length between an alkyne and a tether atom was so important to obtain a successful result. Especially, the chain length between the internal alkyne

Table 5. Rh(I)-catalyzed intermolecular [4+2+2] cycloaddition.[a]



Entry	Reactant			Time [h]	Yield [%][b]	
		n	R		**b**	**c**
1	**25a**	1	Ph		-	70 (**25c**)
2	**26a**	1		6 h	65 (**26b**)	20 (**26c**)
3	**27a**	1		6 h	59 (**27b**)	28 (**27c**)
4	**28a**	2		24 h	95 (**28b**)	3 (**28c**)
5	**29a**	1		12 h	-	53 (**29c**)
6	**30a**	2		24 h	-	48 (**30c**)

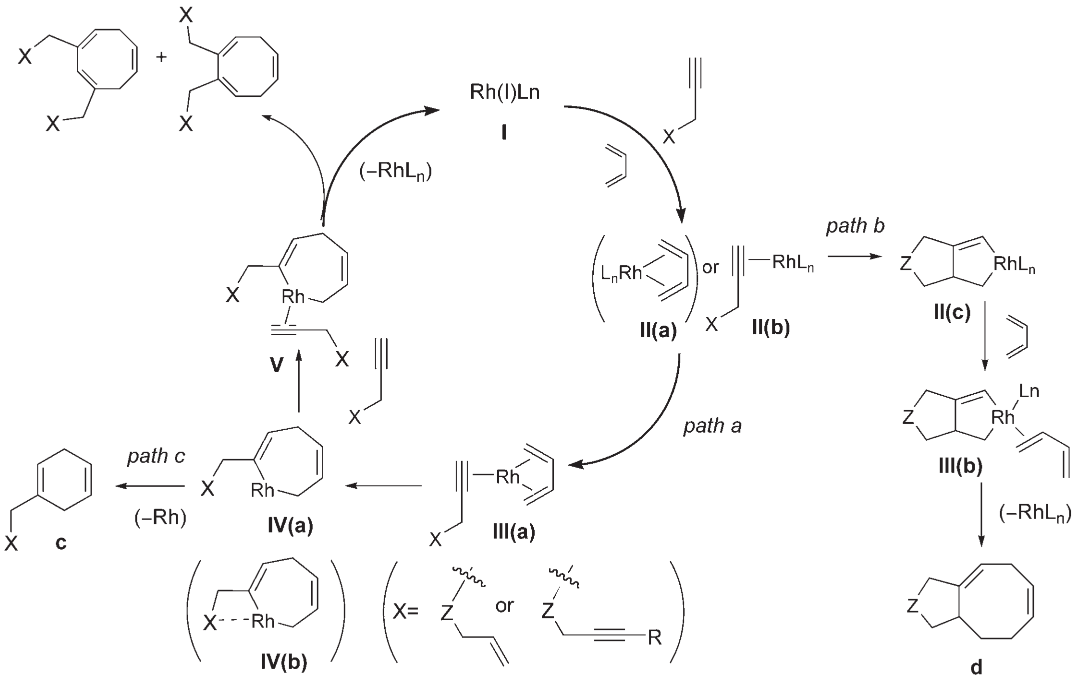
[a] 0.8 mmol of reactant, 2.5 mol% $[Rh(cod)Cl]_2$ (10 mg), and 5 mol% AgOTf (10 mg) were reacted in 3 mL toluene at room temperature.

[b] Isolated yield.

and a tether atom plays a critical role in the cycloaddition.

On the basis of these data, a simplified reaction mechanism for the [4+2+2] cycloaddition of two enynes (or two diynes) with one diene has been drawn in Scheme 1.

A catalytic rhodium species may react with butadiene or enyne (or diyne) to form rhodium com-



Scheme 1.

plex(es), **IIa**, and/or **IIb**, depending upon the reaction conditions. When **IIb** follows path "b", **d** will be formed.[5 h] Reaction of **IIa** with enyne (or diyne) or of **IIb** with butadiene will lead to the same intermediate **IIIa**. The reason for the formation of **IIIa** deduced from experimental observation was as follows: the reaction product was insensitive to the order of the addition of enyne and butadiene. Formation of metallacycle, **IVa**, followed by demetallation will lead to a [4+2] cycloaddition product, **c**. Addition of another enyne to **IVa** followed by migratory insertion and reductive elimination affords the [4+2+2] cycloaddition products, **b** and **b′**. Although, the mechanism has been proposed it is, however, too crude to explain the observed regioselectivity and the effect of the slow addition of reactants on the regioselectivity. We have to wait further study to explain the observed regioselectivity.

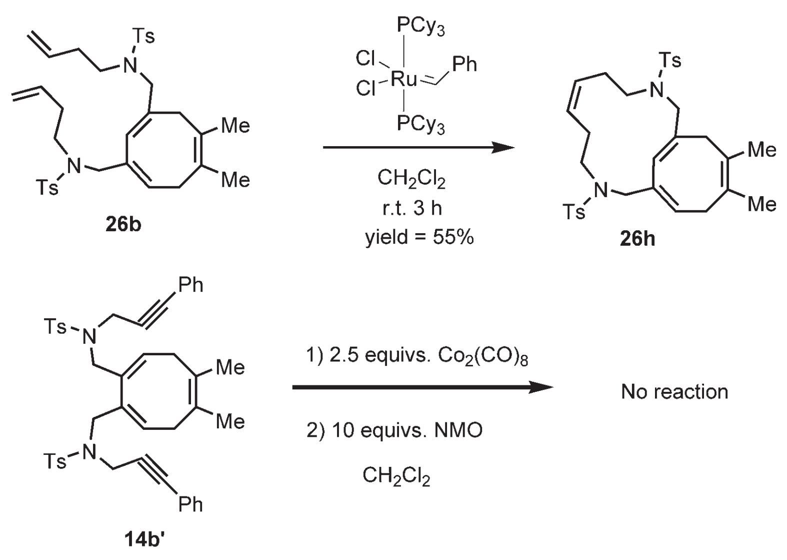
Further Synthetic Reactions of Eight-Membered Compounds

The synthetic versatility of the eight-membered products bearing alkenyl or alkynyl side chains was examined (Scheme 2).

In order to unify the terminal olefins using the ring-closing metathesis, **26b** was treated with the first generation Grubbs catalyst to give a medium-sized bicyclic compound. After the reaction, a bicyclo[10.5.1]octadecatetraene derivative **26g** was isolated in 55% yield, with a *trans/cis* ratio of 3.2:1. The methodology used in this study provides a facile route to macrocyclic compounds. For the alkynyl side chains, we planned to do a Pauson–Khand reaction or a PtCl$_2$-catalyzed skeletal reorganization between the double bond on the 8-membered ring and the triple bond on the side chain. However, all attempts to do a Pauson–Khand reaction of **14b′** were unsuccessful. Further studies on the use of the eight-membered ring compounds are in progress in our laboratory.

Conclusions

We have developed a new intermolecular [Rh(cod)Cl]$_2$/AgX-catalyzed [4+2+2] cycloaddition reaction between two enynes with one diene, and between two diynes and one diene. This is the first example of a rhodium-catalyzed, trimolecular and three-component [4+2+2] cycloaddition to form eight-membered ring compounds. The yield of the reaction was highly dependent upon the counteranion and the reaction medium. It is noteworthy for the cycloaddition of two enynes and one diene that only one regioisomer was obtained, at least in some cases. However, the regioselectivities for the cycloaddition of two diynes with one diene were rather poor. The use of a syringe pump in the slow addition of reactants slightly enhanced the regioselectivity. A further study will shed light on a more realistic reaction mechanism and provide some ways to improve the regioselectivity of the cycloaddition reaction. In the near future, we hope that addition of our method to the repertoire of eight-membered ring compound production expands the synthetic application of cycloaddition reactions. In addition, the [4+2+2] cycloaddition product between two enynes and one diene was subjected to ring-closing metathesis yielding the corresponding bicyclic tetraene in one synthetic step. Interestingly, the cycloadducts between two diynes and one diene were rather inert to further reactions. Current efforts in our



Scheme 2.

laboratory are directed towards a deeper understanding of the mechanism and a synthetic application of this new type of reaction.

Experimental Section

General Remarks

All reactions were performed under an atmosphere of nitrogen unless stated otherwise. Work-up procedures for the cycloaddition were done in air. All solvents were dried and distilled according to standard methods before use. Liquids were transferred *via* a syringe or cannula. TLC plates were visualized by ultraviolet light and treatment with acidic *p*-anisaldehyde stain followed by gentle heating. Infrared spectra were recorded on a Shimadzu IR-470 spectrometer as films on NaCl by evaporation of a solvent or in $CHCl_3$ solution. ^{1}H NMR and ^{13}C NMR spectra were obtained with a Bruker 300 spectrometer. All NMR samples were run in $CDCl_3$ and chemical shifts are expressed in terms of $Si(Me)_4$. High resolution mass spectrum was measured at the Korea Basic Science Institute (Daegu).

General Procedures for Rhodium-Catalyzed Three-Component Tri-Molecular [4+2+2] Cycloaddition of Enynes (Diynes)

To a flame-dried Schlenk flask (15 mL) capped with a rubber septum, 5 mL of toluene were injected *via* a syringe under an N_2 flow. 2.5 mol% of $[Rh(COD)Cl]_2$ and 5 mol% of AgOTf were added sequentially. After the Rh catalyst solution had been stirred for 10 min, 1.0 mmol of diene (1.5 equivs.) was injected by using a 1 mL syringe. 0.73 mmol of enyne (or diyne) was put in under an N_2 flow. Then the reaction was monitored by a thin-layer chromatography (TLC). After the reactant had disappeared, the solvent was removed under reduced pressure and flash chromatography of the residue on a silica gel column eluting with hexane and ethyl acetate (v/v, 10:1) gave the product.

Compound 1b: ^{1}H NMR ($CDCl_3$, 600 MHz): $\delta = 1.70$ (s, 3H), 1.80 (s, 3H), 2.40 (s, 3H), 2.42 (s, 3H), 2.63 (d, $J = 7.6$ Hz, 2H), 2.77 (s, 2H), 3.71 (s, 2H), 3.73 (d, $J = 6.5$ Hz, 2H), 3.75 (s, 2H), 3.76 (d, $J = 6.5$ Hz, 2H), 5.05–5.16 (m, 4H), 5.38 (t, $J = 7.6$ Hz, 1H), 5.37–5.40 (m, 2H), 5.84 (s, 1H), 7.27 (d, $J = 7.9$ Hz, 2H), 7.31 (d, $J = 7.9$ Hz, 2H), 7.66 (d, $J = 7.9$ Hz, 2H), 7.70 (d, $J = 7.9$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 175 MHz): $\delta = 21.6$, 21.6, 22.9, 23.1, 35.9, 36.1, 49.3, 49.7, 51.0, 52.7, 119.2, 119.7, 124.6, 124.8, 125.5, 127.1, 127.2, 127.3, 129.7, 129.8, 132.0, 132.4, 135.3, 135.9, 137.5, 137.73, 143.26, 143.34; EI-MS: calcd. exact mass for $C_{32}H_{40}N_2S_2O_4$: 580.2429, found: 580.2423.

Compound 1b′: ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.72$ (s, 6H), 2.42 (s, 6H), 2.62 (d, $J = 7.6$ Hz, 4H), 3.77 (d, $J = 6.4$ Hz, 4H), 4.01 (s, 4H), 5.11–5.05 (m, 4H), 5.45 (m, 2H), 5.48 (t, $J = 7.6$ Hz, 2H), 7.28 (d, $J = 8.2$ Hz, 4H), 7.76 (d, $J = 8.2$ Hz, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 21.8$, 23.4, 35.7, 49.2, 50.0, 119.5, 125.1, 127.6, 127.7, 129.8, 132.3, 135.3, 137.5, 143.3; EI-MS: calcd. exact mass for $C_{32}H_{40}N_2S_2O_4$: 580.2429, found: 580.2423.

Supporting Information

Characterization data of the other new compounds.

Acknowledgements

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