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Rh(I)-catalyzed mild intramolecular [4+2] cycloaddition reactions of ester-tethered diene-yne compounds

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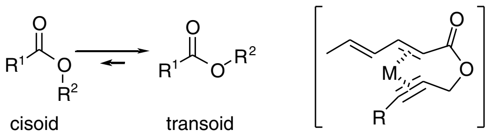
Abstract—The cationic rhodium(I) species derived from $[Rh(COD)Cl]_2$ and $AgSbF_6$ efficiently catalyze intramolecular [4+2] cycloadditions of ester-tethered 1,3-diene-8-yne derivatives such as 2-propynyl penta-2,4-dienoate and 2,4-pentadienyl propiolate derivatives in fluorinated alcohols.

Bicyclic lactones are important constituents of many natural products that have significant biological activities.[1,2] The straightforward procedure for preparing these lactones is the intramolecular Diels–Alder (IMDA) reaction of ester-tethered diene-yne or diene-ene substrates.[3] In general, however, the IMDA reaction of the ester-tethered compounds requires a high reaction temperature or a prolonged reaction time.[4–6] Furthermore, Lewis acids that are effective in activating α,β-unsaturated ester dienophiles are not necessarily efficient in the IMDA reaction of the ester-tethered compounds.[4a,7] The low IMDA reactivity of the esters-tethered reactants is a result of difficulty in adopting a cisoid form in which the reactive sites are in close proximity. This conformational difficulty is due to the steric repulsion between two substituents (R^1 and R^2) and the dipole–dipole repulsion between carbonyl and ethereal oxygen groups (Scheme 1).[8]



Scheme 1.

To overcome the conformational disadvantage of the ester-tethered compounds for the IMDA reaction, we have developed the preparation of bis-aluminated triflic amide as a bidentate Lewis acid, and reported the efficient formation of oxabicyclo[4.4.0]decane compounds in good yields under mild conditions through the IMDA reaction of 3,5-hexadienyl acrylate derivatives.[9] The bidentate Lewis acid, however, did not work for the IMDA reaction of 2,4-pentadienyl acrylate derivatives that would afford oxabicyclo[4.3.0]nonane derivatives.

Recent advances in transition metal-catalyzed chemistries prompted us to examine the formation of oxabicyclo[4.3.0]nonane derivatives through intramolecular [4+2] cycloadditions of ester-tethered diene-yne compounds. Transition metal-catalyzed intramolecular cycloadditions of diene-alkene or diene-alkyne compounds have been proven to be useful for the preparation of bicyclocarbocyclic compounds.[10] It has also been reported that rhodium[11] and palladium[12]-catalyzed reactions have shown their potential efficiency to form lactone. Although Rh(I)-catalyzed intramolecular [4+2] cycloadditions of ω-alkynyl diene compounds have been studied by many groups,[13,14] to our knowledge, there is no report about the transition metal-catalyzed cycloaddition of the ester-tethered diene-yne compounds. Since transition metals form complexes with carbon–carbon unsaturated bonds, the estertethered diene-yne compounds such as 2-propynyl penta-2,4-dienoate[15] and 2,4-pentadienyl propiolate derivatives would take a preferable cisoid form (Scheme 1). Thus,

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Keywords: Rhodium catalyst; Cycloaddition; Ester-tethered diene-yne.

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the formation of oxabicyclo [4.3.0]nonane derivatives would be expected to occur under mild conditions by the treatment of the ester-tethered diene-yne compounds with a transition metal catalyst.[16,17] We describe herein the first successful Rh(I)-catalyzed intramolecular [4+2] cycloadditions of ester-tethered diene-yne compounds.

At the outset, it soon turns out that the Rh(I)-catalyzed reaction of 2-butynyl sorbate (**1a**) under the conditions reported for the intramolecular [4+2] cycloadditions of ω-alkynyl dienes ended with the recovery or the hydrolysis of **1a** depending on the employed Rh(I)-catalyst.[13,18] Treatment of **1a**, however, with the cationic rhodium(I) catalyst[13d] derived from $[Rh(COD)Cl]_2$ (5 mol %) and $AgSbF_6$ (13 mol %) in 1,2-dichloroethane or dichloromethane at room temperature for 12 h gave benzofuranone **3a** in 11% or 10% yield, which would be generated by the dehydrogenation of adduct **2a** during the work-up (Table 1, entries 1 and 2).

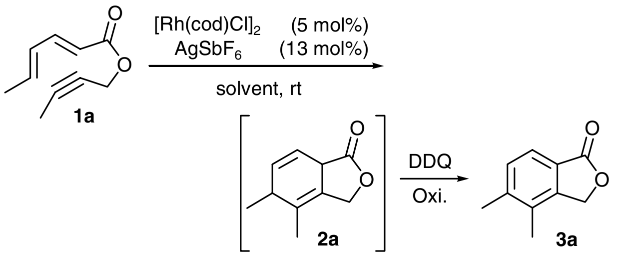
As in the reaction exemplified by Livinghouse,[13a,d] fluorinated alcohols showed a significant acceleration in the rate of the cyclization. Thus, with the use of trifluoroethanol (TFE), **1a** was consumed at room temperature within 7 h giving rise to a mixture of products **2a** and **3a** in 51% and 13% yields (by ^{1}H NMR analysis), respectively (entry 3). However, ethanol was totally ineffective for the cyclization (entry 5).[19] Since the primarily formed **2a** was readily oxidized to **3a** during the work-up and was difficult to be separated from **3a**, the crude reaction mixture was directly treated with DDQ. Thus, after the DDQ oxidative work-up, **3a** was isolated in 58% yield (entry 3). Hexafluoroisopropanol (HFIP) is also the preferable solvent for the formation of **2a** (entry 4). It is worth noting that the addition of phosphine ligand (Ph_3P, dppb, or $((CF_3)_2CHO)_3P$) to the cationic Rh-catalyst or the sole use of $AgSbF_6$ without the use of Rh-catalyst did not yield **2a**. It should also be mentioned that the reaction of **1a** in TFE or HFIP at refluxing temperature without the use of the catalyst did not give the cyclization product.

Based on the described results, the cationic Rh(I)-catalyzed intramolecular [4+2] cycloadditions of sorbate derivatives **1a–d** were carried out in TFE or HFIP, and the results are shown in Table 2.

Thus, the cationic Rh(I) catalyst worked nicely in the reaction of **1b** to give **3b** in 81% yield after the aforementioned DDQ oxidation work-up (method **A**) (Table 2, entry 1). The addition of silica gel to the reaction mixture after the consumption of **1b** (by TLC) and the subsequent isolation of the crude product (method **B**) gave conjugated dienelactone **4** in 76% yield (entry 2). By applying method **B** to the reaction of **1a**, conjugated lactone **5** was obtained as a single isomer in 67% yield (entry 5). This indicates that primarily formed **2a** or **2b** isomerizes to dienelactone **4** or **5** by the addition of silica gel. It is interesting to note that the reaction of **1c** or **1d** is more efficient in TFE than in HFIP (entries 6–9).

The efficiency of TFE was found remarkable in the intramolecular [4+2] cycloadditions of propiolate **6** (Table 3). Thus, in the presence of the cationic Rh(I) catalyst, the reaction of propiolate **6a** proceeded at room temperature within 1 h to give corresponding adduct **7a** in a quantitative yield (entry 1). In contrast to **1**, the use of HFIP as a solvent lowered the yield of **7a** due to the decomposition of **6a** (entries 2 and 3). In the cases of methyl- and phenyl-substituted compounds **6b** and **6c**, TFE was also found to be an efficient solvent, and adducts **7b** and **7c** were obtained in excellent yields, respectively (entries 5 and 7). In all cases examined, each adduct **7a–c** was obtained as a single isomer with the illustrated trans stereochemistry. Although the thermal IMDA reactions of **6** in the absence of the cationic Rh(I) catalyst showed excellent results, a higher temperature and longer time is necessary for the completion of the reaction (by TLC) (Table 3, entries 4, 6, and 8).

Table 1. Effective solvent on the [4+2] cycloaddition of **1a**



Entry	Solvent	Time (h)	Crude (%)[a]	Yield (%)[b]	
				3a	**1a**
1	$(CH_2Cl)_2$	12	—	11[c]	20
2	CH_2Cl_2	12	—	10[c]	23
3	TFE	7	**2a** (51) **3a** (13)	58	—
4	HFIP	5	**2a** (74) **3a** (11)	67	—
5[d]	EtOH	18	—	—	57

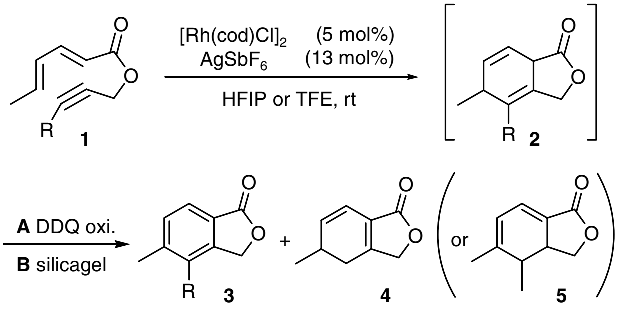
[a] Yield in parantheses was determined by ^{1}H NMR with toluene as an internal standard, before DDQ oxidation.

[b] Isolated yield.

[c] Compound **3a** was isolated without treatment with DDQ due to no detection of **2a** in the crude.

[d] Reaction temperature; 60 °C.

Table 2. Rh(I)-catalyzed intramolecular [4+2] cycloadditions of **1**[a]



Entry	**1**	R	Solvent	Time (h)	Method[b]	Yield (%)[c]	
						3	**4** or **5**
1	**1b**	H	HFIP	1	**A**	81	—
2	**1b**	H	HFIP	1	**B**	—	**4** 76
3	**1b**	H	TFE	4	**B**	3	**4** 66
4	**1a**	Me	HFIP	5	**A**	67	—
5	**1a**	Me	HFIP	5	**B**	—	**5** 67
6[d]	**1c**	Ph	HFIP	22	**A**	11	—
7	**1c**	Ph	TFE	27	**A**	63	—
8[d]	**1d**	TBS	HFIP	27	**A**	14	—
9[e]	**1d**	TBS	TFE	48	**A**	51	—

[a] [Rh(cod)Cl]$_2$; 5 mol %, AgSbF$_6$; 13 mol %.

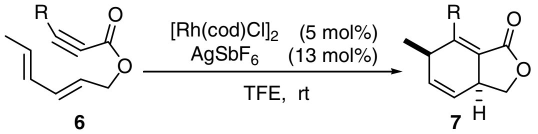
[b] Method A: After usual work-up, the crude was treated with DDQ. Method B: After the starting material **1** was consumed, the reaction mixture was treated with silica gel for 1 h.

[c] Isolated yield.

[d] Reaction temperature; reflux. Consumption of the staring material was scarcely observed at rt.

[e] Reaction temperature; 50 °C.

Table 3. Rh(I) catalyzed [4+2] cycloaddition of propiolate **6**[a]



Entry	**6**	R	Solvent	Time (h)	**7** (%)[b]
1	**6a**	H	TFE	1	Quant.
2	**6a**	H	HFIP	1	11
3	**6a**	H	HFIP–CH$_2$Cl$_2$	1	73
4[c]	**6a**	H	Toluene	12	94
5	**6b**	Me	TFE	1	98
6[c,d]	**6b**	Me	Xylene	24	96
7	**6c**	Ph	TFE	2	Quant.
8[c]	**6c**	Ph	Xylene	3	98

[a] [Rh(cod)Cl]$_2$; 5 mol %, AgSbF$_6$; 13 mol %.

[b] Isolated yield.

[c] The thermal reaction was caried out under refluxing conditions in the absence of the Rh-catalyst.

[d] See, Ref. 16a.

It should also be mentioned that the formation of oxabicyclo[4.4.0]decane derivatives by the reaction of 3-butynyl sorbate or 3,5-hexadienyl propiolate was not observed under the aforementioned cationic Rh(I)-catalyzed conditions.

On the basis of previous reports about the transition metal-catalyzed [4+2] cycloaddition[13,14] or the ene-reaction,[11] a plausible catalytic cycle for the present cationic Rh(I)-catalyzed intramolecular [4+2] cycloaddition of the ester-tethered diene-yne compounds **6** is shown in Figure 1. That is, the formation of metalacyclic intermediate **B** via complex **A** and the reductive elimination of Rh(I) gave cycloadduct **7**. The analogous catalytic cycle is considered to be involved in the reactions of **1**. Although the significant effect of the fluorinated alcohols for the present reaction is quite notable, no clear advantage to the use of TFE was reported in cationic Rh(I)-catalyzed cyclizations of 1,3-diene-8-yne derivatives.[13c] At present, we considered that the fluorinated alocohols might increase the cisoid conformation of **1** or **6** by the polar effect (Scheme 1)[20]

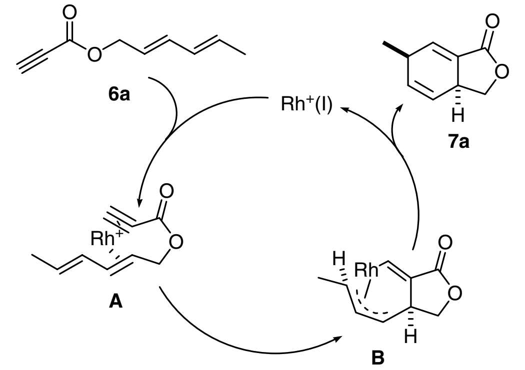


Figure 1. A catalytic cycle.

and/or accelerate in the generation and reactivity of the cationic Rh(I) catalyst, which coordinates to unsaturated bonds.[21] The adverse effect caused by the addition of phosphine ligands would be a result of a decrease in the electorophilicity of cationic Rh(I) by coordination of the added phosphine ligand to the cationic metal center.

In conclusion, we demonstrated that the intramolecular [4+2] cycloaddition reaction of ester-tethered diene-yne compounds was catalyzed by the cationic Rh(I) species derived from $[Rh(COD)Cl]_2$ and $AgSbF_6$ in fluorinated alcohols. To the best of our knowledge, this is the first example of the transition metal-catalyzed intramolecular [4+2] cycloadditions of ester-tethered diene-yne compounds. We believe that the present reactions of ester-tethered ene-yne derivatives raise new possibilities for the formation of bicyclic lactone compounds under mild conditions. Further studies on the reactivity of ester-tethered diene-yne compounds are underway.

Acknowledgments

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References and notes

1. (a) Fallis, A. G. *Acc. Chem. Res.* **1999**, *32*, 464–474; (b) Suzuki, Y.; Murata, T.; Takao, K.; Tadano, K. *Synth. Org. Chem. Jpn.* **2002**, *60*, 679–689.
2. (a) Chackalamannil, S.; Davies, R. J.; Wang, Y.; Asberom, T.; Doller, D.; Wong, J.; Leon, D. *J. Org. Chem.* **1999**, *64*, 1932; (b) Jauch, J. *Angew. Chem., Int. Ed.* **2000**, *39*, 2764; (c) Padwa, A.; Brodney, M. A.; Dimitroff, M.; Liu, B.; Wu, T. *J. Org. Chem.* **2001**, *66*, 3119; (d) Suzuki, Y.; Ohara, A.; Sugaya, K.; Takao, K.; Tadano, K. *Tetrahedron* **2001**, *57*, 7291; (e) Wong, L. S.-M.; Sherburn, M. S. *Org. Lett.* **2003**, *5*, 3603; (f) Inoue, M.; Sato, T.; Hirama, M. *J. Am. Chem. Soc.* **2003**, *125*, 10772.
3. Reviews on intramolecular Diels–Alder reaction: (a) Ciganek, E. In *Organic Reactions*; Dauben, W. G., Ed.; John Wiley & Sons: New York, 1984; Vol. 32, pp 1–374; (b) Craig, D. *Chem. Soc. Rev.* **1987**, *16*, 187; (c) Roush, W. R. In *Advances in Cycliaddition*; Curran, D. P., Ed.; JAI Press: Greenwich, CT, 1990; Vol. 2, pp 91–146; (d) Roush, W. R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, UK, 1991; Vol. 5, pp 513–550.
4. The recent examples on IMDA reactions of 3,5-hexadienyl acrylate derivatives, see: (a) Jung, M. E.; Huang, A.; Johnson, T. W. *Org. Lett.* **2000**, *2*, 1835; (b) Kim, P.; Nantz, M.; Kurth, M. J.; Olmsteas, M. M. *Org. Lett.* **2000**, *2*, 1831; (c) Jones, G. A.; Paddon-Row, M. N.; Sherburn, M. S.; Turner, C. I. *Org. Lett.* **2002**, *4*, 3789.
5. The recent examples on IMDA reactions of 2,4-pentadienyl acrylate derivatives, see: (a) Turner, C. I.; Wong, L. S.-M.; Turner, P.; Paddon-Row, M. N.; Sherburn, M. S. *Chem. Eur. J.* **2002**, *8*, 739; (b) Turner, C. I.; Paddon-Row, M. N.; Moran, D.; Payne, A. D.; Sherburn, M. S.; Turner, P. *J. Org. Chem.* **2005**, *70*, 5561.
6. 2-Propenyl sorbate gave the IMDA product under hursh conditions (250 °C, 120 h). 3-Butenyl sorbate derivatives failed to give cyclized products even at 275 °C, see: Martin, S. F.; Williamson, S. A.; Gist, R. P.; Smith, K. M. *J. Org. Chem.* **1983**, *48*, 5170.
7. Toyota, M.; Wada, Y.; Fukumoto, K. *Heterocycles* **1993**, *35*, 111–114.
8. (a) Cain, D.; Pawar, D. M.; Stewart, M.; Billings, H., Jr.; Noe, E. A. *J. Org. Chem.* **2001**, *66*, 6092; Review on the conformation and stereoelectronic effect of ester compounds, see: (b) Deslongchamps, P. In *Stereoelectric Effects in Organic Chemistry*; Pergamon Press: Oxford, 1983; pp 54–100.
9. (a) Saito, A.; Ito, H.; Taguchi, T. *Org. Lett.* **2002**, *4*, 4619; (b) Saito, A.; Yanai, H.; Taguchi, T. *Tetrahedron* **2004**, *60*, 12239; (c) Saito, A.; Yanai, H.; Taguchi, T. *Tetrahedron Lett.* **2004**, *45*, 9439.
10. Reviews on transition metal catalyzed cyclization: (a) Trost, B. M. *Acc. Chem. Res.* **1990**, *23*, 34; (b) Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635; (c) Trost, B. M.; Krische, M. J. *Synlett* **1998**, 1; (d) Trost, B. M. *Chem. Rev.* **2001**, *101*, 2067; (e) Aubert, C.; Buisine, O.; Malacria, M. *Chem. Rev.* **2002**, *102*, 813.
11. (a) Lei, A.; He, M.; Zhang, X. *J. Am. Chem. Soc.* **2002**, *124*, 8198; (b) Tong, X.; Zhang, Z.; Zhang, X. *J. Am. Chem. Soc.* **2003**, *125*, 6370; (c) He, M.; Lei, A.; Zhang, X. *Tetrahedron Lett.* **2005**, *46*, 1823.
12. (a) Ma, S.; Lu, X. *J. Org. Chem.* **1991**, *56*, 5120; (b) Zhang, Q.; Lu, X. *J. Am. Chem. Soc.* **2000**, *122*, 7604; (c) Jia, C.; Piao, D.; Kitamura, T.; Fujiwara, Y. *J. Org. Chem.* **2000**, *65*, 7516.
13. (a) Jolly, R. S.; Luedtke, G.; Sheehan, D.; Livinghouse, T. *J. Am. Chem. Soc.* **1990**, *112*, 4965; (b) Wender, P. A.; Jenkins, T. E.; Suzuki, S. *J. Am. Chem. Soc.* **1995**, *117*, 1843; (c) Gilbertson, S. R.; Hoge, G.; Genov, D. G. *J. Org. Chem.* **1998**, *63*, 1007; (d) O'Mahony, D. J. R.; Belanger, D. B.; Livinghouse, T. *Synlett* **1998**, 443; (e) Motoda, D.; Kinoshita, H.; Shinokubo, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2004**, *43*, 1860.
14. Ni-Catalyzed intramolecular [4+2] cycloaddition reaction of ω-alkynyl dienes, see: Wender, P. A.; Jenkins, T. E. *J. Am. Chem. Soc.* **1989**, *111*, 6432.
15. To our knowledge, no examples of 2-propynyl penta-2,4-dienoate derivatives have been reported. On the attempted thermal reactions of 2- or 3-alcoxycarbonyl-2-propenyl penta-2,4-dienoates, see: (a) Boeckman, R. K., Jr.; Demko, D. M. *J. Org. Chem.* **1982**, *47*, 1789; (b) Mulzer, J.; Bock, H.; Eck, W.; Buschmann, J.; Luger, P. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 414; (c) Ishihara, J.; Miyakawa, J.; Tsujimoto, T.; Murai, A. *Synlett* **1997**, *12*, 1417.

16. Thermal reactions of 2,4-pentadienyl propiolates, see: (a) White, J. D.; Sheldon, B. G. *J. Org. Chem.* **1981**, *46*, 2273; (b) Birtwhistle, D. H.; Brown, J. M.; Foxton, M. W. *Tetrahedron* **1998**, *44*, 7309; (c) Turner, C. I.; Williamson, R. M.; Paddon-Row, M. N.; Sherburn, M. S. *J. Org. Chem.* **2001**, *66*, 3963; (d) Pradilla, R. F.; Baile, R.; Tortosa, S. *Chem. Commun.* **2003**, 2476.
17. $Pd(OAc)_2/LiCl$-Catalyzed reaction of 2,4-pentadienyl propiolate derivatives has been reported to give intramolecular carbochlorination products, see: Nilsson, Y. I. M.; Gatti, R. G. P.; Andersson, P. G.; Backvall, J. E. *Tetrahedron* **1996**, *52*, 7511.
18. Recovery of **1a**: $(Ph_3P)_3RhCl$/TFE, $[((CF_3)_2CHO)_3P]_2$-RhOTf/THF, and $[Rh(DIPHOS)(CH_2Cl_2)]SbF_6/CH_2Cl_2$. Hydrolysis of **1a**: $[RhCl(NBD)_2]_2$, SDS/H_2O.
19. Neither THF nor acetone were effective sovents for the cyclization. The reason for the difference in the efficiency of the fluorinated alcohols and the other polar solvents is unclear.
20. It has been reported that the polar solvent such as, H_2O or DMSO is highly efficient in intramolecular cyclizations of ester compounds. (a) Jung, M. E. *Synlett* **1999**, 843; (b) Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Synlett* **2002**, 674; (c) Yanai, H.; Saito, A.; Taguchi, T. *Tetrahedron* **2005**, *61*, 7987.
21. Rhodium chloride complex such as Willkinson's catalyst accelerates the [4+2] cycloadditon of 1,3-diene-8-yne or 1,3,8-triene derivatives in TFE. It has been suggested that TFE enhances the polarizability of the Rh–Cl bond. See, Refs. 13a and 13d.