



# Ru-Catalyzed cycloisomerization of $\delta$ -enallenes to form cyclic 1,3-dienes or 1,4-dienes

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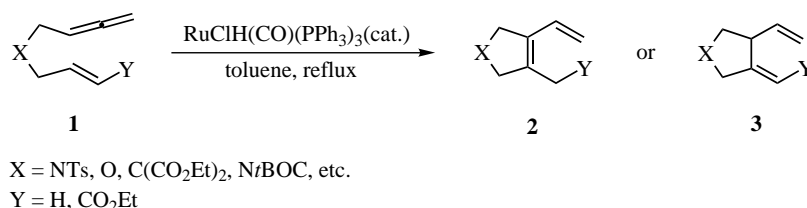
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**Abstract**—RuClH(CO)(PPh<sub>3</sub>)<sub>3</sub>-catalyzed cycloisomerization of  $\delta$ -enallenes to afford the cyclized 1,3- and 1,4-dienes depending on the substrates and reaction conditions is described by reacting  $\delta$ -enallenes in toluene at reflux. © 2002 Elsevier Science Ltd. All rights reserved.

The development of efficient chemical transformation which involves the reactants corresponds exactly to empirical formula of the products is highly desirable in organic synthesis due to the atom economy, which avoids the amount of chemicals and waste.<sup>1,2</sup> Intramolecular coupling and cyclization of the tethered alkenes and alkynes to produce cyclic 1,4-dienes involving catalytic cycloisomerization represent the reactions that meet such a goal.<sup>3</sup> Although the late transition metal-catalyzed intramolecular cycloisomerization of enynes and dienes has been known,<sup>4,5</sup> only the Ni/Cr-catalyzed cycloisomerization of  $\delta$ -enallenes to give 1,4-dienes is known by Trost et al.<sup>6</sup> Recently Mori et al.<sup>7</sup> reported the Ru-catalyzed cycloisomerization of enynes with RuClH(CO)(PPh<sub>3</sub>)<sub>3</sub>. In our ongoing studies to utilize allene substrates in organic synthesis, we have found that the ruthenium-catalyzed cycloisomerization of  $\delta$ -enallenes afforded the cyclized 1,3- or 1,4-dienes depending on the substrates and/or reaction conditions, which is shown in Scheme 1.

The results of Ru-catalyzed cycloisomerization of  $\delta$ -enallenes to form 1,3- or 1,4-cyclic dienes are summa-

rized in Table 1. To find optimum conditions, allenyl- and allyl-substituted *p*-toluenesulfonamide **1a** was used as a model compound. As a RuH source, RuClH(CO)(PPh<sub>3</sub>)<sub>3</sub> and RuH<sub>2</sub>(CO)(PPh<sub>3</sub>)<sub>3</sub> were tested and RuClH(CO)(PPh<sub>3</sub>)<sub>3</sub> was better in the terms of yield. Of the solvents tested dioxane, DMF, CH<sub>3</sub>CN, THF and toluene, toluene was the best of choice. The enallene **1a** reacted with RuClH(CO)(PPh<sub>3</sub>)<sub>3</sub> (5 mol%) in toluene at reflux for 8 h to afford 1,3-cyclic diene **2a** in 60% isolated yield (entry 1 in Table 1). Under the same conditions  $\delta$ -allenyl  $\alpha$ ,  $\beta$ -unsaturated ester **1b** was cycloisomerized to  $\beta$ , $\gamma$ -unsaturated ester **2b** in 66% yield (entry 2). In contrast to sulfonamide **1a** when *t*BOC-substituted allenyl allylamide **1c** was treated under the same conditions to afford 1,4-cyclic diene **3a**<sup>8</sup> in 56% yield (entry 3). The malonate branched enallene **1d** was cycloisomerized to 1,3-cyclic diene **2c**<sup>9</sup> in 58% yield (entry 4).<sup>10</sup> For the  $\delta$ -enallene diol **1e** refluxing for 7 h afforded the 1,4-cyclic diene **3b** (entry 5). However,  $\delta$ -enallene diol **1e** was heated for a prolonged time (12 h) 1,3-cyclic diene **2d** was afforded as a sole product (entry 6). The dibenzoate **1f** was isomerized to 1,3-cyclic diene **2e** as the only product in 75% yield (entry

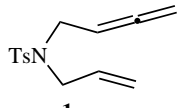
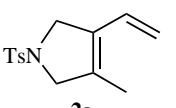
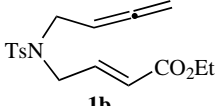
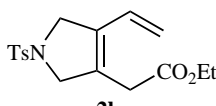
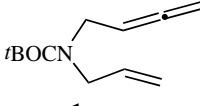
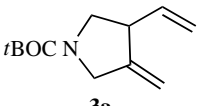
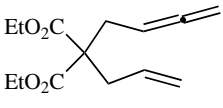
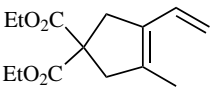
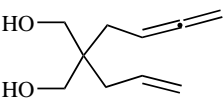
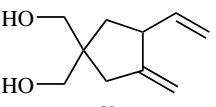
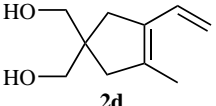
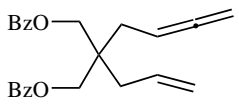
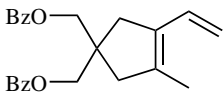
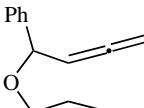
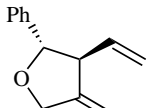
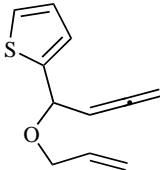
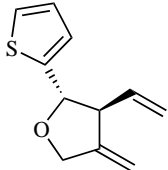


## Scheme 1.

**Keywords:** cyclization; dienes;  $\delta$ -enallenes; isomerization; ruthenium-catalyst.

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**Table 1.** Ru-catalyzed cycloisomerization of  $\delta$ -enallenes<sup>a</sup>

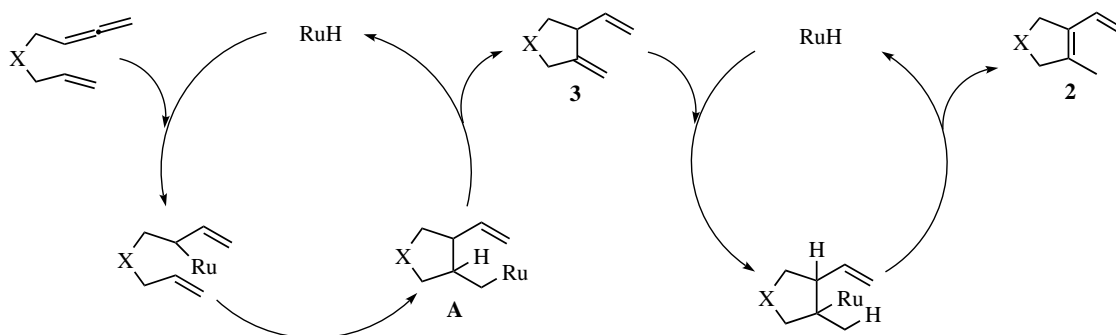
Entry	$\delta$ -Enallenes	Time (h)	Product	Isolated Yield (%) <sup>b, c</sup>
1	 <b>1a</b>	8	 <b>2a</b>	60
2	 <b>1b</b>	2	 <b>2b</b>	66
3	 <b>1c</b>	3	 <b>3a</b>	56
4	 <b>1d</b>	14	 <b>2c</b>	58
5	 <b>1e</b>	7	 <b>3b</b>	60
6	<b>1e</b>	12	 <b>2d</b>	69
7	 <b>1f</b>	3	 <b>2e</b>	75
8	 <b>1g</b>	3	 <b>3c</b>	71 ( <i>trans</i> : <i>cis</i> = 11 : 1)
9	 <b>1h</b>	6	 <b>3d</b>	64 ( <i>trans</i> : <i>cis</i> = 6.4 : 1)

<sup>a</sup>The reaction were run with  $\delta$ -enallenes and  $\text{RuClH}(\text{CO})(\text{PPh}_3)_3$  (5 mol %) in the toluene at reflux.

<sup>b</sup>Separated by  $\text{SiO}_2$  column chromatography. <sup>c</sup>The ratios of *trans* : *cis* were determined by  $^1\text{H}$  NMR spectra.

7). This method was applied to  $\alpha$ -substituted  $\delta$ -enallene. Treatment of  $\alpha$ -phenyl-substituted enallene **1g** the *trans*-1,4-cyclic diene **3c**<sup>11</sup> as a major product was obtained in 71% yield (entry 8). Finally,  $\alpha$ -2-thienyl-substituted enallene **1h** was readily isomerized to the *trans*-1,4-cyclic diene **3d** as the major component in 64% yield (entry 9).<sup>12</sup>

The typical procedure is as follows. A solution of enallene **1a** (50 mg, 0.19 mmol) in toluene (3 ml) was added  $\text{RuClH}(\text{CO})(\text{PPh}_3)_3$  (9 mg, 0.01 mmol) and the mixture was heated at reflux for 8 h. Toluene was evaporated in vacuo and the crude product was separated by  $\text{SiO}_2$  column chromatography (hexanes:ethyl acetate=1:5) to afford the product **2a** (30 mg, 60%).



Scheme 2.

The plausible mechanism for the formation of 1,3- or 1,4-cyclic dienes from  $\delta$ -enallenes can be envisioned as shown in Scheme 2. It is presumed that hydorruthenation of  $\delta$ -enallene **1** followed by intramolecular olefin addition gives ruthenium complex **A**. A *syn*  $\beta$ -H elimination of **A** would produce 1,4-cyclic dienes **3**. Further hydorruthenation of **3** followed by  $\beta$ -H elimination could give 1,3-cyclic dienes **2** (Scheme 2).

In summary, the ruthenium-catalyzed cycloisomerization of  $\delta$ -enallenes to form the cyclic 1,3- or 1,4-dienes depending on the substrates was accomplished.

### Acknowledgements

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### References

1. Trost, B. M. *Science* **1991**, *254*, 1471–1477.
2. (a) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259–281; (b) Trost, B. M.; Krische, M. J. *Synlett* **1998**, 1–16.
3. Reviews: (a) Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635–662; (b) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49–92; (c) Malacria, M. *Chem. Rev.* **1996**, *96*, 289–306.
4. For the cycloisomerization of enynes: Pd, review: (a) Trost, B. M. *Acc. Chem. Res.* **1990**, *23*, 34–42; (b) Trost, B. M.; Trost, M. K. *J. Am. Chem. Soc.* **1991**, *113*, 1850–1852; (c) Trost, B. M.; Lautens, M. J. *Am. Chem. Soc.* **1985**, *107*, 1781–1783; (d) Trost, B. M.; Romero, D. L.; Rise, F. *J. Am. Chem. Soc.* **1994**, *116*, 4268–4278; (e) Trost, B. M.; Haffner, C. D.; Jebaratnam, D. J.; Krische, M. J.; Thomas, A. P. *J. Am. Chem. Soc.* **1999**, *121*, 6183–6192; (f) Trost, B. M.; Krische, M. J. *J. Am. Chem. Soc.* **1996**, *118*, 233–234; (g) Trost, B. M.; Phan, L. T. *Tetrahedron Lett.* **1993**, *34*, 4735–4738; (h) Boger, D. L.; Tarby, C. M.; Myers, P. L.; Caporale, L. H. *J. Am. Chem. Soc.* **1996**, *118*, 2109–2110. Ru: (i) Le Paih, J.; Rodríguez, D. C.; Dérien, S.; Dixneuf, P. H. *Synlett* **2000**, 95–97; (j) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2000**, *122*, 714–715; (k) Mori, M.; Kozawa, Y.; Nishida, M.; Kanamaru, M.; Onozuka, K.; Takimoto, M. *Org. Lett.* **2000**, *2*, 3245–3247.
5. For the cycloisomerization of dienes, Pd: (a) Kisanga, P.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2000**, *122*, 10017–10026; (b) Bray, K. L.; Lloyd-Jones, G. C. *Eur. J. Org. Chem.* **2001**, 1635–1642; (c) Bothe, U.; Rudbeck, H. C.; Tanner, D.; Johannsen, M. *J. Chem. Soc., Perkin Trans. 1* **2001**, 3305–3311. Ti: (d) Okamoto, S.; Livinghouse, T. *Organometallics* **2000**, *19*, 1449–1451; (e) Okamoto, S.; Livinghouse, T. *J. Am. Chem. Soc.* **2000**, *122*, 1223–1224. Ru: (f) Yamamoto, Y.; Nakagai, Y.-I.; Ohkoshi, N.; Itoh, K. *J. Am. Chem. Soc.* **2001**, *123*, 6372–6380; (g) Yamamoto, Y.; Ohkoshi, N.; Kameda, M.; Itoh, K.; *J. Org. Chem.* **1999**, *64*, 2178–2179.
6. Trost, B. M.; Tour, J. M. *J. Am. Chem. Soc.* **1988**, *110*, 5231–5233.
7. Nishida, M.; Adachi, N.; Onozuka, K.; Matsumura, H.; Mori, M. *J. Org. Chem.* **1998**, *63*, 9158–9159.
8. Oppolzer, W.; Birkinshaw, T. N.; Bernardinelli, G. *Tetrahedron Lett.* **1990**, *31*, 6995–6998.
9. Chatani, N.; Morimoto, T.; Muto, T.; Murai, S. *J. Am. Chem. Soc.* **1994**, *116*, 6049–6050.
10. Refluxing **1d** in toluene for 7 h afforded 1:1 mixture of 1,4-diene and starting **1d** without formation of 1,3-diene **2c**.
11. Mikami, K.; Nakai, T.; Matsueda, H.; Sato, H.; Kurosumi, A. Japan Kokai Tokyo Koho, 1992, JP 04211074. (*Chem. Abstr.* **1992**, *118*, 254734).
12. Selected physical and spectral data are as follows. **2a**:  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  1.70 (s, 3H), 2.43 (s, 3H), 4.08 (s, 2H), 4.21 (s, 2H), 4.96 (d, 1H,  $J=17.6$  Hz), 5.12 (d, 1H,  $J=10.6$  Hz), 6.43 (dd, 1H,  $J=17.6, 10.6$  Hz), 7.32 (d, 2H,  $J=8.1$  Hz), 7.74 (d, 2H,  $J=8.1$  Hz);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  144.1, 134.8, 132.3, 130.5, 130.1, 128.3, 128.2, 115.9, 59.9, 55.4, 22.2, 12.1; HRMS (EI)  $m/z$  263.0980 (calcd for  $\text{C}_{14}\text{H}_{17}\text{NO}_2\text{S}$  263.0980). **3b**:  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  1.32(d, 1H,  $J=13.2$  Hz), 1.34 (d, 1H,  $J=13.2$  Hz), 1.98 (dd, 2H,  $J=12.8, 8.4$  Hz), 3.14 (dt, 1H,  $J=8.1, 8.4$  Hz), 3.65 (m, 4H), 4.81 (m, 1H), 4.94 (m, 1H), 5.05 (m, 2H), 5.67 (ddd, 1H,  $J=16.9, 10.3, 8.1$  Hz);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  153.1, 140.7, 115.5, 108.2, 71.4, 69.1, 47.5, 47.2, 39.1, 38.3; HRMS (EI)  $m/z$  168.1198 (calcd for  $\text{C}_{10}\text{H}_{16}\text{O}_2$  168.1150). **2d**:  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  1.76 (s, 3H), 2.30 (s, 2H), 2.33 (s,

2H), 2.57 (bs, 2H), 3.68 (s, 2H), 3.69 (s, 2H), 5.01 (d, 1H,  $J=17.2$  Hz), 5.03 (d, 1H,  $J=10.6$  Hz), 6.62 (dd, 1H,  $J=17.2, 10.6$  Hz);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  134.5, 130.3, 129.2, 111.2, 68.5, 43.7, 43.2, 36.6, 12.2; HRMS (EI)  $m/z$  168.1200 (calcd for  $\text{C}_{10}\text{H}_{16}\text{O}_2$  168.1150). **3d** (ca. 6.4:1 mixture of *trans* and *cis*):  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  3.28 (m, 0.86H), 3.60 (m, 0.14H), 4.46 (ddt, 0.86H,  $J=13.2, 2.6, 2.2$  Hz), 4.54 (ddt, 0.14H,  $J=13.2, 1.1, 2.2$  Hz), 4.66 (ddt, 0.14H,  $J=13.2, 1.8, 2.2$  Hz), 4.68 (ddt, 0.86H,  $J=13.2, 1.1, 2.2$  Hz), 4.79 (d, 0.86H,  $J=9.2$  Hz), 4.95 (dt, 0.86H,

$J=2.6, 2.2$  Hz), 4.99 (dt, 0.14H,  $J=2.6, 2.2$  Hz), 5.03 (dt, 1H,  $J=2.6, 2.2$  Hz), 5.12 (dd, 1H,  $J=17.2, 1.5$  Hz), 5.22 (dd, 1H,  $J=10.3, 1.5$  Hz), 5.27 (ddd, 0.14H,  $J=17.2, 10.3, 8.8$  Hz), 5.40 (d, 0.14H,  $J=8.8$  Hz), 5.68 (ddd, 0.86H,  $J=17.2, 10.3, 8.4$  Hz), 6.91 (m, 0.14H), 6.95 (dd, 1H,  $J=5.1, 3.7$  Hz), 7.02 (m, 0.86H), 7.22 (dd, 0.14H,  $J=5.1, 1.1$  Hz), 7.27 (dd, 0.86H,  $J=5.1, 1.1$  Hz);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  149.5, 147.1, 133.9, 131.8, 125.8, 124.2, 124.1, 118.6, 116.2, 107.4, 105.0, 81.0, 78.3, 70.4, 69.2, 56.9, 48.2; HRMS (EI)  $m/z$  192.0601 (calcd for  $\text{C}_{11}\text{H}_{12}\text{OS}$  192.0609).