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RHODIUM-CATALYZED CYCLOISOMERIZATION OF ALLYL PROPARGYL ETHERS: AN EFFICIENT SYNTHESIS OF 3,4-DISUBSTITUTED FURANS

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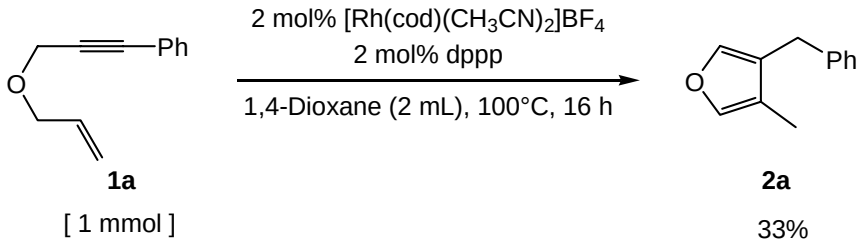
Abstract – Cycloisomerization of allyl propargyl ethers was found to be catalyzed by a cationic rhodium complex to give 3,4-disubstituted furans in one step. Addition of carboxylic acids to the reaction improved the yield of the products. Generation of a rhodium hydride species from a rhodium complex with the carboxylic acids followed by hydrorhodation of the substrate with the rhodium hydride species would be involved in the reaction pathway.

Transition metal-catalyzed cyclization of enynes provides an efficient and useful method for the construction of ring systems. It has been known that 1,6-enynes are highly reactive compounds for cyclization and effective substrate for five-membered ring compounds.[1-3] Cyclization of allyl propargyl ethers has been reported to give 3,4-dialkylidenetetrahydrofurans,[4] 3-alkenyl-4-alkylidenetetrahydrofurans,[4a,5] or 3-alkenyl-2,5-dihydrofurans.[6] If the hydrogen transfer takes place after the cyclization, it becomes a good synthetic method for functionalized furans. There has been only one example for such cycloisomerization, in which, however, a furan derivative is obtained as a by-product in low yield.[7] Herein we report on a rhodium-catalyzed cycloisomerization of allyl propargyl ethers that provides 3,4-disubstituted furans selectively in one step.

Treatment of allyl 3-phenyl-2-propynyl ether (**1a**) with 2 mol% of $[Rh(cod)(MeCN)_2]BF_4$ in 1,4-dioxane at 100°C for 16 h gave 3-benzyl-4-methylfuran (**2a**) in 33% isolated yield (Scheme 1). The choice of the cationic rhodium complex and appropriate bidentate phosphine ligands such as dppp was essential for the success of this transformation. It is noteworthy that the *exo*-methylene type product was not detected at all in this reaction.

This paper is dedicated to Professor Barry M. Trost on the occasion of his 65th birthday.



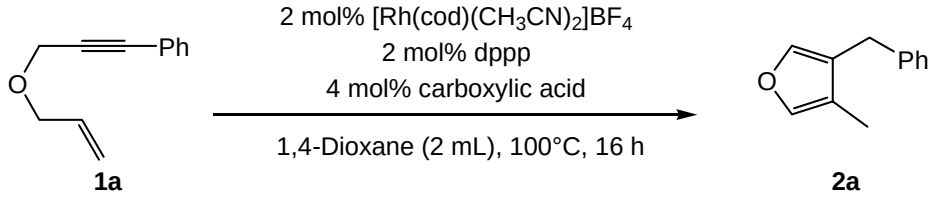
1a
[1 mmol]

2a
33%

Scheme 1

On the basis of assumption that a rhodium hydride species is an active catalytic species in this cycloisomerization, we examined various carboxylic acids as additives, which produce Rh(III)-H species by oxidative addition to Rh(I).[4b,8] The effect of various carboxylic acids in this reaction is shown in Table 1. In all cases examined, improvement of the yield was observed (Entries 1-4). In particular, the yield was increased to 64% when 10 mol% of acetic acid was added to the reaction (Entry 5). However, the reaction did not proceed when acetic acid was used as solvent (Entry 6). A large excess of acetic acid appeared to deactivate the catalyst.

Table 1. Effect of various carboxylic acids



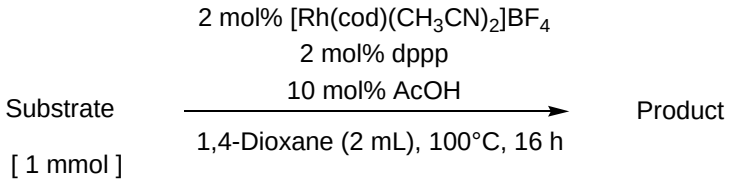
1a
[1 mmol]

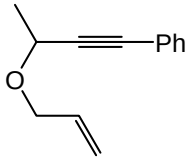
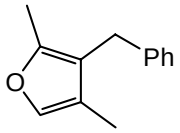
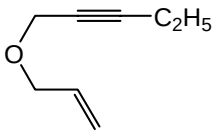
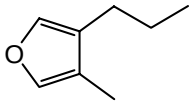
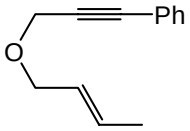
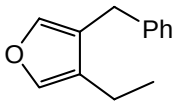
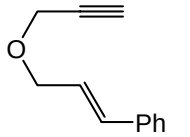
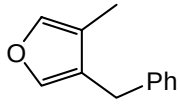
2a

Entry	Carboxylic acids	Yield (%) of **2a**
1	HCOOH	49
2	AcOH	61
3	PhCOOH	50
4	CF_3COOH	44
5	AcOH (10 mol%)	64
6	AcOH (Solvent)	n.r.

The scope of the rhodium-catalyzed cycloisomerization of allyl propargyl ethers is shown in Table 2. The cycloisomerization of **1b** having a substituent on the propargylic position also proceeded giving the corresponding 2,3,4-trisubstituted furan (**2b**) in 35% yield (Entry 1). The reaction of substrate (**1c**) having an ethyl group at the alkyne terminal gave the product (**2c**) in a lower yield of 20% (Entry 2).[9] However, the reaction of substrates (**1d**) and (**1e**) having a substituent at the olefin terminal did not give any

Table 2. Rh-catalyzed cycloisomerization of allyl propargyl ethers

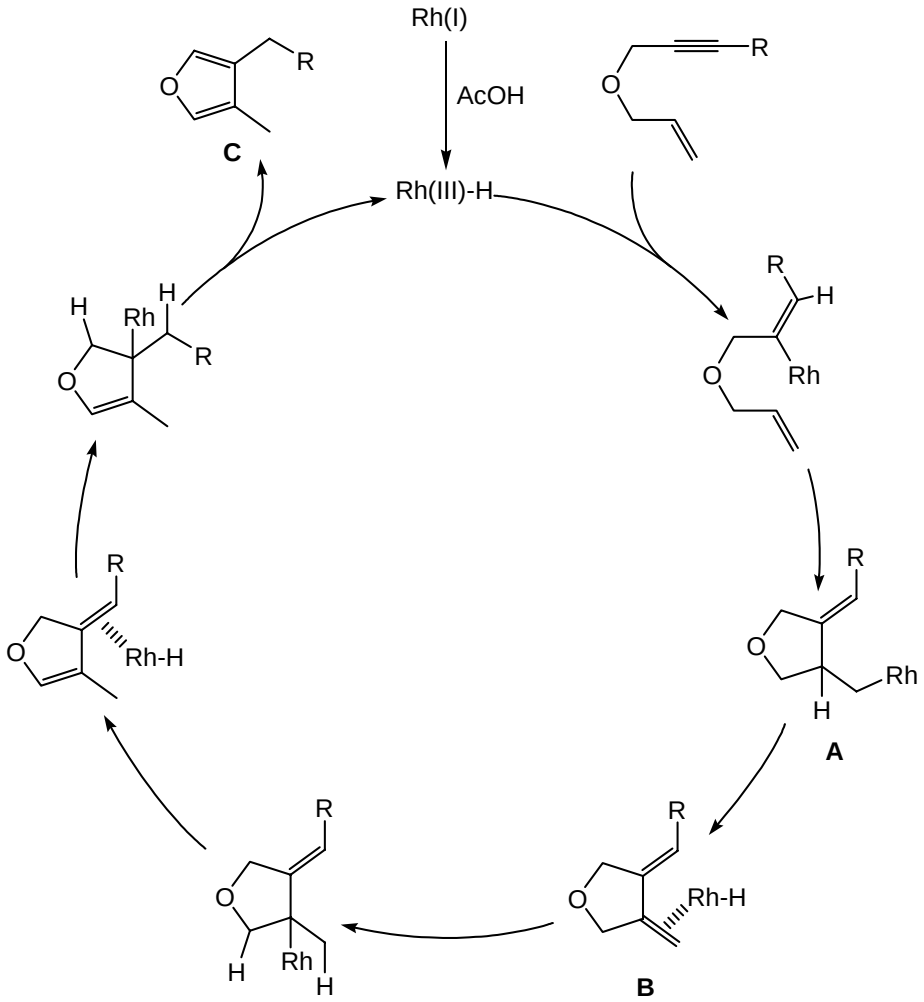


Entry	Substrate		Product		Yield, %
1		**1b**		**2b**	35
2		**1c**		**2c**	20
3		**1d**		**2d**	0
4		**1e**		**2a**	0

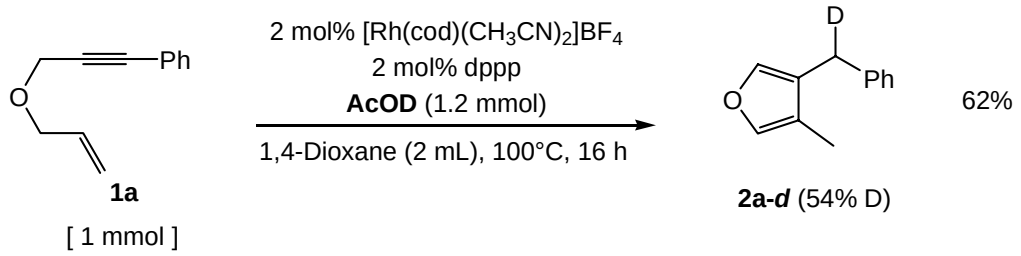
cyclized product. Steric hindrance of the substituent at the olefin terminal would prevent the cyclization (Entries 3 and 4).

Scheme 2 shows a plausible reaction mechanism for the cycloisomerization. Initially, oxidative addition of AcOH to Rh(I) complex generates Rh(III)-H species as an active catalytic species. Addition of the resulting Rh(III)-H species to the triple bond followed by insertion of the olefin moiety to Rh-C bond generates an intermediate (**A**). β-Hydride elimination affords an *exo*-methylene type compound (**B**). Then repetition of addition and elimination of Rh(III)-H causes the isomerization of double bond, which finally results in the formation of the product furan (**C**). Since we did not observe the formation of the *exo*-methylene type product (**B**), the isomerization of the double bond would proceed much faster than the cyclization.

The label experiment of **1a** was performed using 1.2 equiv. of AcOD (Scheme 3). As a result, deuterized **2a-*d*** (54% D) at the benzylic position was obtained in 62% yield. This result supports the mechanism involving the generation of Rh-D species from Rh(I) complex and AcOD followed by the deuteriorhodation of the triple bond.



Scheme 2. Plausible mechanism for Rh-catalyzed cycloisomerization of allyl propargyl ethers



Scheme 3. Label experiment

In conclusion, cycloisomerization of allyl propargyl ethers catalyzed by the cationic rhodium complex gave 3,4-disubstituted furans selectively in one step. This method provides a convenient synthetic route to highly substituted furans.

REFERENCES AND NOTES

1. B. M. Trost, *Acc. Chem. Res.*, 1990, **23**, 34.

2. B. M. Trost and M. J. Krische, *Synlett*, 1998, 1.

3. C. Aubert, O. Buisine, and M. Malacria, *Chem. Rev*., 2002, **102**, 813.

4. (a) B. M. Trost, E. D. Edstrom, and M. B. Carter-Petillo, *J. Org. Chem*., 1989, **54**, 4489. (b) B. M. Trost, D. L. Romero, and F. Rise, *J. Am. Chem, Soc*., 1994, **116**, 4268. (c) J. Le Paih, D. C. Rodríguez, S. Dérien, and P. H. Dixneuf, *Synlett*, 2000, 95. (d) N. Chatani, H. Inoue, T. Morimoto, T. Muto, and S. Murai, *J. Org. Chem*., 2001, **66**, 4433.

5. (a) B. M. Trost and F. D. Toste, *J. Am. Chem, Soc*., 2000, **122**, 714. (b) P. Cao, B. Wang, and X. Zhang, *J. Am. Chem, Soc*., 2000, **122,** 6490.

6. (a) M. Mori, N. Sakakibara, and A. Kinoshita, *J. Org. Chem*., 1998, **63**, 6082. (b) L. Ackermann, C. Bruneau, and P. H. Dixneuf, *Synlett*, 2001, 397.

7. J.-F. Nguefack, V. Bolitt, and D. Sinou, *Tetrahedron Lett*., 1996, **37**, 5527.

8. (a) B. M. Trost, D. C. Lee, and F. Rise, *Tetrahedron Lett.*, 1989, **30**, 651. (b) B. M. Trost and D. C. Lee, *J. Org. Chem.*, 1989, **54**, 2271.

9. **2a:** ^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) 7.29-7.26 (m, 2H), 7.20-7.19 (m, 3H), 7.17 (s, 1H), 7.10 (s, 1H), 3.71 (s, 2H), 1.86 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ (ppm) 140.2, 139.9, 139.8, 128.5, 128.3, 126.0, 124.4, 120.3, 29.8, 8.1. IR (neat): 2921, 1451, 1142, 1045, 786, 715, cm^{-1}. K. Inomata, Y. Nakayama, M. Tsutsumi, and H. Kotake, *Heterocycles*, 1979, **12**, 1467. **2b:** ^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) 7.23 (t, *J*=7.5 Hz, 2H), 7.17 (t, *J*=7.5 Hz, 1H), 7.13 (d, *J*=7.5 Hz, 2H), 7.06 (s, 1H), 3.68 (s, 2H), 2.21 (s, 2H), 1.79 (s, 3H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ (ppm) 148.5, 140.5, 136.7, 128.3, 128.1, 125.8, 120.9, 117.9, 29.4, 11.8, 8.6. IR (neat): 2920, 1494, 1450, 1123, 738, 713 cm^{-1}. Y. Fujita and T. Nakai, *Synthesis*, 1983, 997. **2c:** ^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) 7.14 (s, 1H), 7.13 (s, 1H), 2.31 (t, *J*=7.5 Hz, 2H), 1.95 (s, 3H), 1.56 (sext, *J*=7.5 Hz, 2H), 0.96 (t, *J*=7.5 Hz, 3H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ (ppm) 139.2, 139.0, 125.4, 120.1, 25.6, 22.5, 14.0, 8.1. IR (neat): 2959, 1459, 1141, 1048, 878, 782 cm^{-1}. HRMS (EI). Calcd for $C_8H_{12}O$ 124.0888 (M^+). Found 124.0887.