Ruthenium-Catalyzed Transformation of 3-Benzyl But-1-ynyl Ethers into 1,3-Dienes and Benzaldehyde via Transfer Hydrogen

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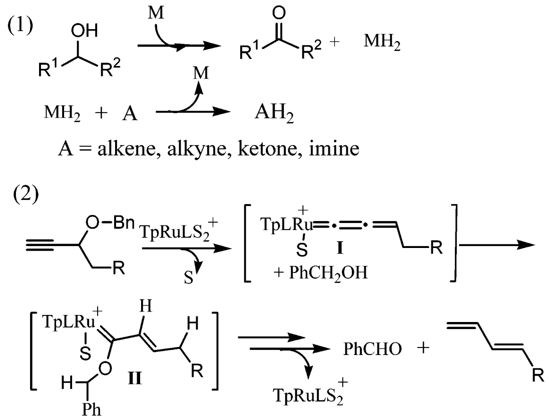
$TpRuPPh_3(CH_3CN)_2PF_6$ catalyzed the transformation of various 3-benzyl but-1-ynyl ethers into dienes and benzaldehyde at a catalyst loading of 5 mol %. This process represents an atypical pattern of transfer hydrogenation. This catalytic reaction can be applied to various derivatives of 2-ethynyl tetrahydrofurans and pyrans to cleave their ether rings and gives diene and tethered aldehyde functionalities, respectively.

Metal-catalyzed transfer hydrogenation between two organic molecules has attracted considerable attention.[1−4] This process is considered to be environmentally friendly because it avoids the use of oxidants and reductants. Several useful catalytic reactions have been designed on the basis of this process, and notable examples include the asymmetric hydrogenation of ketones and imines from 2-propanol and formic acids using chiral metal catalysts.[1a,2a,b] Scheme 1 (eq 1) shows a typical pattern for most cases of metal-catalyzed transfer hydrogenation which involves the hydrogenation of C = X (X = O, NR, CR_2) or alkyne by alcohols and formic acid.[1−3] We sought to identify a new pathway to broaden the present scope. Benzyl ethers have been widely used as a protecting group for organic alcohols,[5,6] and the removal of this functionality relies on an excess (>1.0 equimolar) of suitable oxidants or reductants. Chemical degradation of this protecting group using a metal catalyst alone is a challenging problem in synthetic chemistry.

SCHEME 1



Recently, we reported an interesting degradation of ethynyl benzyl ethers via metal-catalyzed transfer hydrogenation.[7] As shown in Scheme 1 (eq 2), the ethers are transformed into benzaldehyde and dienes using $TpRuPPh_3(CH_3CN)_2PF_6$ catalyst (8.0 mol %). We propose a plausible mechanism on the basis of deuterium-labeling experiments. The reaction is initiated by formation of ruthenium−allenylidenium species **I**,[8] which subsequently formed ruthenium−oxacarbenium **II** and ultimately gave diene and benzaldehyde in good yields. This process provides easy access to organic dienes from readily available ethynyl alcohols. In this study, we report an improvement in the catalyst efficiency as well as the catalytic application to the ring cleavage of 2-ethynyltetrahydrofuran and -pyran derivatives.

We first examined the catalytic transformation of benzyl ether **1** with various catalysts, and the results are summarized in Scheme 1. We selected $TpRuPPh_3(CH_3CN)_2PF_6$[9] catalyst (**I**) containing a tris(1-pyrazolyl)borate

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(1) For reviews of ruthenium-catalyzed hydrogen transfer reactions, see: (a) Noyori, R.; Hashiguchi, S. *Acc. Chem. Res.* **1997**, *30*, 97. (b) Naota, T.; Takaya, H.; Murahashi, S. *Chem. Rev.* **1998**, *98*, 2599. (c) Palmer, M. J.; Wills, M. *Tetrahedron: Asymmetry* **1999**, *10*, 2045.

(2) For examples of ruthenium-catalyzed hydrogen transfer reaction, see: (a) Yamada, I.; Noyori, R. *Org. Lett.* **2000**, *2*, 3425. (b) Matsumura, K.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 8738. (c) Gordon, E. M.; Gaba, D. C.; Jebber, K. A.; Zacharias, D. M. *Organometallics* **1993**, *12*, 5020. (d) Wang, G.-Z.; Backvall, J. E. *J. Chem. Soc., Chem. Commun*. **1992**, 980. (e) Mizushima, E.; Yamaguchi, M.; Yamagishi, T. *Chem Lett.* **1997**, 237. (f) Genet, J.-P.; Ratovelomanana-Vidal V.; Pinel, C. *Synlett* **1993**, 478.

(3) For examples of an aluminum-catalyzed reaction (Meerwein−Pondorf−Verley reduction), see: (a) Campbell, E. J.; Zhou, H.; Nguyen, S. T. *Org. Lett.* **2001**, *3*, 2391. (b) Ooi, T.; Miura, T.; Maruoka, K. *Angew. Chem., Int. Ed.* **1998**, *37*, 2347. (c) Ooi, T.; Itagaki, Y.; Miura, T.; Maruoka, K. *Tetrahedron Lett.* **1999**, *40*, 2137. (d) Konishi, K.; Makita, K.; Aida, T.; Inoue, S. *J. Chem. Soc., Chem. Commun*. **1988**, 643.

(4) For hydrogen transfer reaction catalyzed by non-ruthenium transition-metal complexes, see: (a) Muller, D.; Umbricht, G.; Weber, B.; Pfaltz, A. *Helv. Chim. Acta* **1991**, *74*, 232. (b) Gamez, P.; Fache, F.; Lemaire, M. *Tetrahedron: Asymmetry* **1995**, *6*, 705. (c) Evans, D. A.; Nelson, S. G.; Gagne, M. R.; Muci, A. R. *J. Am. Chem. Soc.* **1993**, *115*, 9800.

(5) (a) Czernecki, S.; Georgoulis, C.; Provelenghio, C. *Tetrahedron Lett.* **1976**, 3535 (b) Iwashige, T. Saeki, H. *Chem. Pharm. Bull.* **1967**, *15*, 1803.

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(7) For a preliminary communication, see: Yeh, K. L.; Liu, B.; Lo, C. Y.; Huang, H. L.; Liu, R. S. *J. Am. Chem. Soc.* **2002**, *124*, 6510.

(8) Only several examples are known for nonmetathesis catalytic reactions involving ruthenium−allenylidenium intermediates: (a) Trost, B. M.; Flygare, J. A. *J. Am. Chem. Soc.* **1992**, *114*, 5476. (b) Trost, B. M.; Flygare, J. A. *Tetrahedron Lett.* **1994**, *35*, 4059.

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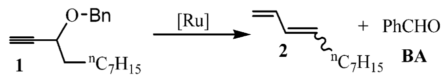
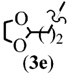
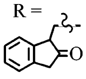
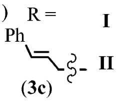
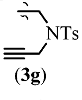
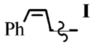
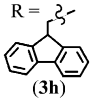
TABLE 1. Catalytic Transformation over Various Solvents and Catalysts



entry	catalyst[a]	solvent	additive	conditions[b]	products[c]
1	**A** (8%)[a]	DCE		80 °C (12 h)	**1** (1.0%), **2** (83%), **BA** (81%)
2	**A** (8%)	benzene		80 °C (12 h)	**1** (68%), **2** (13%), **BA** (18%)
3	**A** (8%)	CH_3CN		80 °C (24 h)	no reaction (**1**, 68%)
4	**A** (8%)	ethyl acetate		80 °C (24 h)	**1** (82%), **2** (9%), **BA** (13%)
5	**A** (8%)	DME		80 °C (24 h)	**1** (77%), **2** (13%), **BA** (15%)
6	**A** (5%)	DCE		80 °C (24 h)	**1** (30%), **2** (47%), **BA** (56%)
7	**A** (5%)	DCE	LiOTf (5%)	80 °C (12 h)	**1** (8%), **2** (23%), **BA** (70%)
8	**A** (5%)	benzene	LiOTf (5%)	80 °C (12 h)	**1** (5%), **2** (78%), **BA** (87%)
9	**A** (5%)	benzene/DCE (1/3)	LiOTf (5%)	80 °C (15 h)	**1** (2%), **2** (86%), **BA** (91%)
10	**A** (5%)	benzene/DCE (3/1)	LiOTf (5%)	80 °C (15 h)	**1** (2%), **2** (84%), **BA** (89%)
11	**B** (5%)	benzene/DCE (3/1)	LiOTf (5%)	80 °C (15 h)	no reaction (**1**, 75%)
12	**C** (5%)	benzene/DCE (3/1)	LiOTf (5%)	80 °C (15 h)	no reaction (**1**, 85%)

[a] Catalyst (mol %): $TpRuPPh_3(CH_3CN)_2PF_6$ (**A**), $TpRuPPh_3(CH_3CN)Cl$ (**B**), $(C_5Me_5)RuPPh_3\,(CH_3CN)_2PF_6$ (**C**). [b] [substrate] = 0.80 M. [c] Yields were obtained after separation from silica column.

TABLE 2. Catalytic Transofrmation of 3-Benzyl But-1-ynyl Ethers

ethers	cond.	diene[d]	BA[e]	ethers	cond.	diene	BA
(1) R = $C_{12}H_{25}$ **(3a)**	I[a]	**4a** (*E/Z*= 7.0, 75%)	86%	(5) R =  **(3e)**	I	**4e** (*E/Z*= 6.3, 69%)	78%
	II[b]	**4a** (*E/Z*= 7.1, 74%)	84%		II	**4e** (*E/Z*= 6.6, 69%)	75%
(2) R = PhC≡CCH_2 **(3b)**	I	**4b** (*E/Z*= 7.0, 70%	76%	(6) R =  **(3f)**	I	**4f** (*E/Z*= 7.1, 79%)	77%
	II	**4b** (*E/Z*= 7.1, 76%)	80%		II	**4f** (*E/Z*= 7.3, 74%)	75%
(3) R =  **(3c)**	I	**4c** (*E/Z*= 8.0, 71%)	77%	(7) R =  **(3g)**	I	**4g** (*E/Z*= 6.5, 85%)	83%
	II	**4c** (*E/Z*= 7.8, 76%)	79%		II	**4g** (*E/Z*= 6.3, 83%)	84%
(4) R =  **(3d)**	I	**4d** (*E/Z*= 7.2, 83%)	85%	(8) R =  **(3h)**	I	**4h** (*E/Z*= 8.4, 76%)	81%
	II	**4d** (*E/Z*= 7.5, 76%)	81%		II	**4h** (*E/Z*= 8.3, 73%)	78%

[a] Condition **I**: 8.0 mol % catalyst **A** in DCE (80 °C, 12 h). [b] **II**: 5 mol % catalyst **A** 5.0 mol % LiOTf in DCE (80 °C, 12 h). [c] **III**: 15 mol % catalyt **A** in DCE (80 °C, 48 h). [d] The yields of diene and benzaldehyde after separation from silica column.

ligand because it readily reacted with a terminal alkyne to form vinylidenium species.[10,11] Among various solvents (entries 1−5), only dichloroethane showed good catalytic activity and gave diene **2** (E/Z = 7.5) in 83% yield in addition to benzaldehyde (81% yield) with 8.0 mol % catalyst **A**. Entries 6−10 show our efforts to enhance the catalytic efficiency with less catalyst. In the presence of LiOTf (5.0 mol %) and 5 mol % catalyst **A**, diene **2** was obtained in only 23% in dichloroethane despite nearly 90% conversion: benzaldehyde was obtained in 70% yield. Diene **2** seemed to be unstable in dichloroethane in the presence of LiOTf additive. Notably, LiOTf shows a significant improvement in catalytic efficiency in benzene, in which diene **2** and benzaldehyde were obtained in respective yields of 78% and 87% yields (entry 8). The use of a mixture of dichloroethane/benzene solvents (entries 9 and 10) gave the best results, with diene **2** obtained in yields as high as 84−86% yields. The catalysts $TpRuPPh_3(CH_3CN)Cl$[9] (**B**) and $C_5Me_5RuPPh_3(CH_3CN)_2PF_6$ (**C**) were inactive even in the presence of LiOTf additive. These results indicate that the two vacant sites and electron-donating ability of the tris(1-pyrazolyl)borate ligand around catalyst **A** are crucial for catalytic activity (Table 1).

We selected benzyl ethers **3a**−**h** to evaluate the catalytic efficiency. The transformations were performed by using either catalyst **A** (8.0 mol %, condition **I**) or a mixture of catalyst **A** (5.0 mol %) and LiOTf (5.0 mol % condition **II**) in hot 1,2-dichloroethane (1.5 M, 80 °C, 12 h). Conditions **I** and **II** gave dienes **4a**−**h** and benzaldehyde in comparable proportions, as shown in Table 2. Entries 1−3 show the application of this reaction to the synthesis of dienes **3a**,**b** bearing a n-$C_{12}H_{25}$ and phenylethynyl group, respectively. We prepared *Z*- and *E*-styryl derivatives **3c** and **3d** (entries 3 and 4) respectively, and the products **4c** and **4d** retained the same configuration. This catalytic process was also suitable to various oxygen- and nitrogen-containing molecules **3e**−**g** (entries 5−7) and gave the corresponding dienes **4e**−**g** and benzaldehyde in reasonable yields. The acidic fluorenyl proton of compound **3h** did not inhibit the catalytic activity, and diene **4h** was obtained in yields of 73−76% (entry 8).

We also prepared various 2-ethynyl cyclic ethers to examine the suitability of this catalytic reaction for cleavage of the ether rings. These ether substrates **5a**−**j** may be used as *E*-(or *Z*-)isomer or a mixture of two isomers depending on their purities after separation from a silica column. As shown in Table 3, these cyclic ethers can be transformed into organic dienes **6a**−**j** bearing a ketone or aldehyde functionality using 10 mol % catalyst **A** in dichloroethane (80 °C, 12 h). Entries 1−4 show successful examples for cleavage of a tetrahydrofuranyl ring via transfer hydrogenation: the products might be either an unconjugated dienyl ketone α or a conjugated

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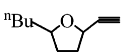
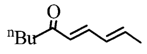
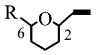
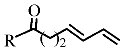
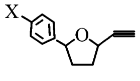
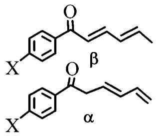
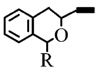
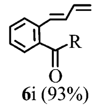
(10) (a) O'Connor, J. M.; Pu, L. *J. Am. Chem. Soc.* **1990**, *112*, 9013. (b) Bianchini, C.; Casares, J. A.; Peruzzini, M.; Romerosa, A.; Zanobini, F. *J. Am. Chem. Soc.* **1996**, *118*, 4585. (c) Knaup, W.; Werner, H. *J. Organomet. Chem.* **1991**, *411*, 471. (d) Chin, C. S.; Chong, D.; Maeng, B.; Ryu, J.; Kim, H.; Kim, M.; Lee, H. *Organometallics* **2002**, *21*, 1739.

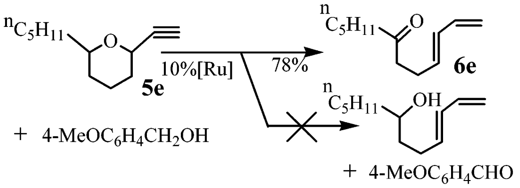
(11) (a) Davies, S. G.; McNally, J. P.; Smallridge, A. *J. Adv. Organomet. Chem.* **1990**, *30*, 30. (b) Werner, H.; Lass, R. W.; Gevert, O.; Wolf, *J. Organometallics* **1997**, *16*, 4077. (c) O'Connor, J. M.; Hiibner, K. *J. Chem. Soc., Chem. Commun.* **1995**, 1209.

TABLE 3. Catalytic Reaction on 2-Ethynyl Cyclic Ethers

ethers	product[a,b]	ethers	products
 (1) **5a** (E/Z=0.57)	 **6a** (89%) (*E/Z*=11.2)	 (5) R=$^{n}C_5H_{11}$(**5e**) (*E/Z*=1.1)	 **6e** (91%) (*E/Z*=25.0)
		(6) R = Ph(**5f**)[d]	**6f** (91%) (*E/Z*=5.3)
(2) X=H (**5b**) (*E* -isomer)	**6b**(β, 93%) (*E/Z*=21.9)	(7) R = PhC≡C(**5g**) (*E/Z*=1.1)	**6g** (87%) (*E/Z*=6.4)
(3) X=OMe(**5c**) (Z-isomer)	**6c**(α, 87%) (*E/Z*=18.8)	(8) R=*E*-PhCH=CH(**5h**) (*E/Z*=1.2)	**6h** (97%) (*E/Z*=5.0)
(4) X=F (**5d**) (Z-isomer)	**6d** (α/β= 3.1, 87%)[a] **6d** (β, 91 %)[c] (*E/Z*=15.8)	 (9) R=H(**5i**)	 **6i** (93%) (*E/Z*=5.2)
		(10) R=Me(**5j**)[e]	**6j** (91%) (*E/Z*=7.5)

[a] 10.0 mol % catalyst, 80 °C, DCE, 12 h. [b] The yields of products were reported after separation from silica column. [c] 80 °C, DCE, 48 h. [d] The structure of this isomer was not available due to the overlap of the H^2 and H^6 NMR resonances. [e] The structure of ether **5j** was not determined.

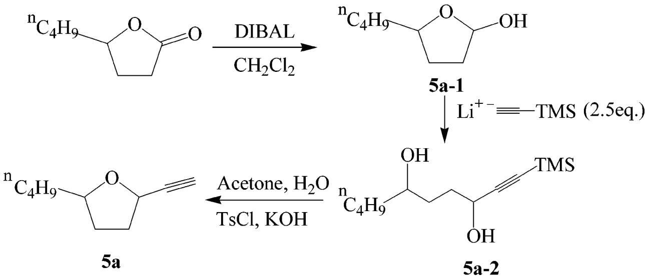
SCHEME 2



isomer *β*, with isolated yields exceeding 87%. Interestingly, the transfer of hydrogenation occurs not only for the benzyl ether derivatives **5b**−**d**, but also to a *n*-butyl ether species **5a**. A similar pattern was observed for 2-ethynyltetrahydropyranyl species **5e**−**h** bearing a 6-substituent like a *n*-pentyl, phenyl, phenylethynyl, or *E*-styryl group. These ethers underwent ring cleavage smoothly to give the corresponding diene ketones **6e**−**f** in excellent yields. This reaction was also applied to bicyclic ethers **5i** and **5j**, which gave aldehydes **6i** and **6j** in respective yields of 93% and 91%. In a separate experiment (Scheme 2), we treated tetrahydrofuranyl derivative **5e** with a better hydrogen donor, *p*-methoxybenzyl alcohol (2.0 equiv), in dichloroethane (80 °C, 12 h). The product consisted mainly of dienyl ketone **6e** rather than dienyl alcohol and *p*-methoxybenzaldehyde. This result suggested that product **6e** was produced from its cyclic ether **5e** via an intramolecular hydrogen transfer process.

In summary, we developed a new catalytic reaction for cleavage of ethynyl benzyl ethers in acyclic and cyclic structural skeletons. These molecules are transformed into organic dienes and benzaldehyde (or ketones) via transfer hydrogen that is beyond the present scope. The catalytic reaction is compatible with suitable oxygen and nitrogen functionalities. Further development of new catalytic reactions on the basis of this pathway is underway.

SCHEME 3



Experimental Section

Trimethylacetylene, benzyl bromide, and other aliphatic aldehydes were obtained commercially and used without purification. 3-Benzyl but-1-ynyl ethers were easily prepared from but-1-yn-3-ol with benzyl bromide in the presence of NaH.[7] $TpRuPPh_3(CH_3CN)_2PF_6$ were prepared by heating $TpRu(PPh_3)_2Cl$ with $LiPF_6$ in CH_3CN according to methods described in the literature.[9] The synthetic protocol and spectral data of compounds **3a**−**c**,**e**−**h** have been reported previously.[7] Spectral data of compounds **3d**, **4d**, **5a**−**j**, and **6a**−**j** in repetitive experiments are provided in the Supporting Information.

Experimental Procedure for the Synthesis of Ethynyl Cyclic Ether 5a. The synthetic scheme is shown in Scheme 3. To a dichloromethane (50 mL) solution of 5-butyldihydrofuran-2-one (5.0 g, 35 mmol) was slowly added DIBAL (42 mL, 42 mmol) at −78 °C, and the mixture was stirred for 1 h before the addition of methanol (20 mL). The solution was passed through a short Al_2O_3 bed to give crude lactol **5a-1** (3.01 g, 21.0 mmol). Compound **5a-1** was added to a THF (100 mL) solution of TMS−C≡CLi (53.0 mmol) at −78 °C. The mixture was stirred for 4 h before being quenched with water (50 mL). The solution was concentrated to ca. 50 mL, extracted with diethyl ether, and eluted through a short silica column to give diol **5a-2** (3.2 g, 13 mmol). To an acetone (40 mL) solution of diol **5a-2** (3.20 g, 13.0 mmol) and toluenesulfonyl chloride (2.60 g, 14.0 mmol) was added an aqueous solution of potassium hydroxide (6.60 mL, 5.0 M). The mixture was stirred for 8 h at 25 °C. The solution was extracted with diethyl ether, concentrated, and eluted through a silica column to afford **5a** (1.30 g, 8.60 mmol) as a mixture of *Z*/*E* isomers.

Experimental Procedures for Catalytic Reactions. Synthesis of Undeca-1,3-diene (2). A long tube containing $TpRu(PPh_3)(CH_3CN)_2PF_6$ (27 mg, 0.035 mmol) was dried in vacuo for 2 h before it was charged with benzyl ether **1** (200 mg, 6.9 mmol) and 1,2-dichloroethane (0.50 mL). The mixture was heated at 80 °C for 12 h before cooling to room temperature. The solution was concentrated and eluted through a silica column (hexane/diether = 5/1) to give diene **2** (88 mg, 5.8 mmol, 83%) and benzaldehyde (60 mg, 5.6 mmol, 81%), respectively: IR (neat, cm^{-1}) 2967 (m), 1658 (w), 1604 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (3 H, t, J = 6.8 Hz), 1.21−1.42 (10 H, m), 2.09 (2 H, q, J = 7.4 Hz), 4.96 (1 H, d, J = 10.0 Hz), 5.09 (1 H, d, J = 16.8 Hz), 5.72 (1 H, dt, J = 15.2 Hz, 6.8 Hz), 6.05 (1 H, m), 6.32 (1 H, dt, J = 17.2 Hz, 10.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 27.7, 29.2, 29.2, 31.8, 32.6, 114.5, 130.8, 135.6, 137.4; HRMS calcd for $C_{11}H_{20}$ 152.1565, found 152.1559.

Acknowledgment. We thank the National Science Council, Taiwan, for supporting this work.

Supporting Information Available: Spectral data of compounds **3d**, **4d**, **5a**−**j**, and **6a**−**j** in repetitive experiments are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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