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Rh-Catalyzed Isomerization and Intramolecular Redox Reaction of Alkynyl Ethers Affording Dihydropyrans and Ketoolefins

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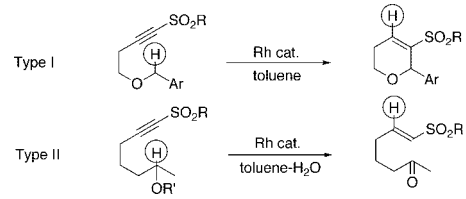
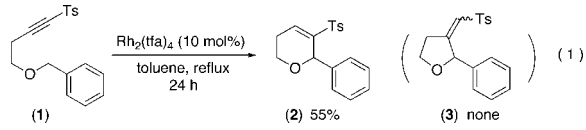
Rh-catalyzed reactions are widely employed in organic synthesis,[1] and a series of reactions dealing with C−H bond activation is one of the most characteristic utilities of this metal species.[1c−i,2] During the course of our study on cyclization of sulfur-functionalized acetylenes with transition metal reagents,[3] we found that a new isomerization reaction from benzyl alkynyl ethers to dihydropyrans (Type I in Scheme 1) and an intramolecular redox reaction from alkynyl ethers to ketoolefins (Type II) are catalyzed by a rhodium salt. These reactions most likely involve cleavage of the C−H bond α to ether in the substrate[4] and subsequent intramolecular transfer of the hydrogen to sulfonylacetylene, yielding products.

Scheme 1. Rh-Catalyzed Transformations of Alkynyl Ethers



In type I reactions, alkynyl benzyl ether **1** (Ts = *p*-$MeC_6H_4SO_2$−) and a catalytic amount of $Rh_2(tfa)_4$ (tfa = CF_3CO_2−) in toluene were heated at reflux to produce the desired dihydropyran **2** in good yield (eq 1). Ring closure proceeded in a highly regioselective manner, and no isomeric five-membered product **3** was detected. The sulfonylacetylene moiety of **1** is critical, because other routine acetylenes having a terminal alkyl, phenyl, trimethylsilyl, or ester (−CO_2Et) group did not yield the desired product.

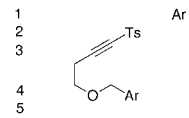
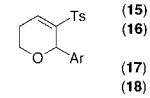
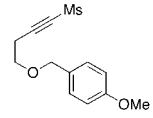
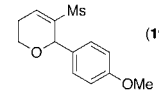
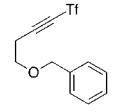
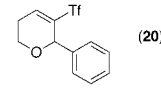
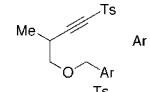
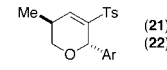
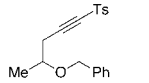
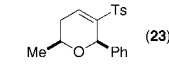
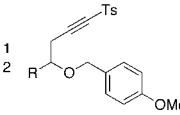
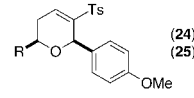


(1)

Table 1 shows more examples of this transformation. Arylmethyl ethers having an electron-rich aromatic ring (**4** and **5** vs **6** and **7**) appear to achieve better product yields (entries 1−5). The load of the catalyst could be reduced to 1 mol% without a significant decrease in the product yields (entry 3). Acetylenes **8** and **9** having a methanesulfonyl (Ms) or trifluoromethanesulfonyl (Tf) group also entered the reaction, to produce **19** and **20** (entries 6 and 7), respectively. Diastereoselective ring closure is also viable as observed in entries 8−12. A substituent at the propargyl position (see **10** and **11**) controls the stereoselection to yield 2,5-*trans*-disubstituted dihydropyrans **21** and **22**, whereas that at the α-carbon of the ether (**12**−**14**) regulates the reaction to form 2,6-*cis*-disubstituted isomers **23**−**25**.[5]

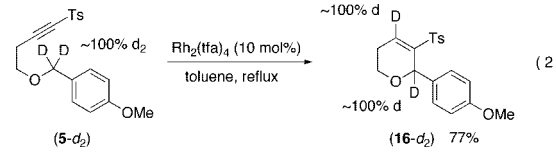
To elucidate the reaction mechanism, deuterium (D)-labeled substrate **5**-d_2 was prepared and submitted to the reaction (eq 2).

Table 1. Preparation of Dihydropyrans According to Eq 1

Entry	Starting Ether			Product[a]		Yield (%)[b]	Ds[c]
1		Ar = Ph	(**1**)		(**2**)	55	
2		*p*-MeC_6H_4-	(**4**)		(**15**)	71	
3		*p*-$MeOC_6H_4$-	(**5**)		(**16**)	78, 76[d], (72[e]), (57[f])	
4		*p*-ClC_6H_4-	(**6**)		(**17**)	51	
5		*p*-BrC_6H_4-	(**7**)		(**18**)	46	
6			(**8**)		(**19**)	90[g]	
7			(**9**)		(**20**)	66[h]	
8		Ar = Ph	(**10**)		(**21**)	46	95: 5
9		*p*-$MeOC_6H_4$-	(**11**)		(**22**)	96	>95: 5
10			(**12**)		(**23**)	60	91: 9
11		R = Ph	(**13**)		(**24**)	59	89:11
12		C_8H_{17}-	(**14**)		(**25**)	76	97: 3

[a] Structure of the major isomer is depicted, where diastereoselectivity is specified. [b] Isolated yields, which are not necessarily optimized. Yields determined by ^{1}H NMR analysis with internal standard are shown in parentheses. [c] Diastereoselectivity determined for a crude sample. [d] Reaction period was 6 h. [e] Catalyst quantity was 5 mol%. [f] Catalyst quantity was 1 mol%. [g] Reaction period was 10 h. [h] Reaction period was 10 h, and the starting material (ca. 20%) remained unchanged.

One of the D atoms was found to migrate cleanly to the vinylic position in **16**-d_2. Thus, we propose the following reaction course (Scheme 2), which consists of (i) coordination of the Rh metal to the acetylenic bond to generate a cationic carbon β to the sulfonyl group (**5**-d_2 → **26** → **27**).[6] (ii) This positive vinyl carbon abstracts the hydrogen α to ether, generating a zwitter ionic intermediate **28**, (iii) which undergoes ring closure to produce the observed product **16**-d_2 (**28** → **29** → **16**-d_2).[7]

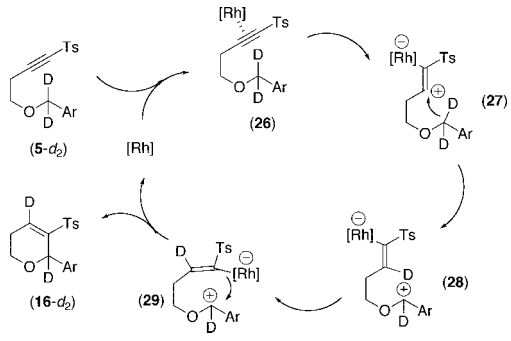


(2)

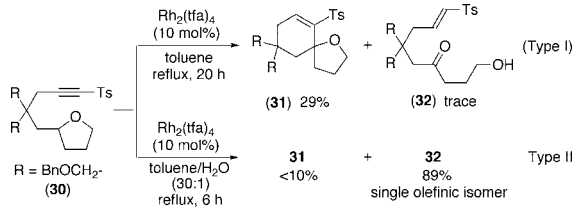
Unlike benzyl ethers, alkyl ether **30** participated in the above cyclization sluggishly, producing a cyclic compound **31** in low yield

10.1021/ja809826a CCC: $40.75

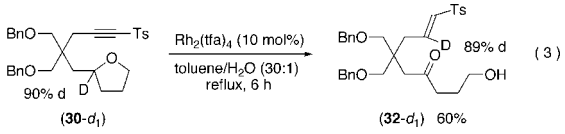
Scheme 2. Proposed Reaction Course



Scheme 3. Type II Reaction of Alkynyl Ether

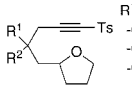
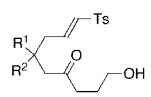
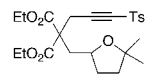
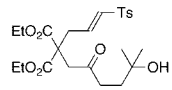
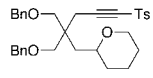
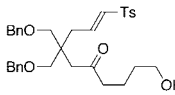
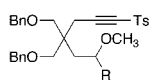
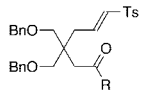


(Type I in Scheme 3). However, when the reaction was performed in wet toluene, a similar C−H bond scission was still operative, and the interception of an intermediate corresponding to **28** in Scheme 2 with water furnished a new product **32** (Type II). This



compound can be considered as a product resulting from an intramolecular reduction (acetylene to olefin) and oxidation (ether to ketone) reaction of alkynyl ether **30**.[8] A separate deuterium label experiment in eq 3 confirmed that the mode of hydrogen migration follows the same manner as that in Scheme 2. Other results of this redox reaction are summarized in Table 2, where usually inert cyclic ethers could be utilized as a synthetic precursor of hydroxy ketones.

Table 2. Redox Reaction from Alkynyl Ethers to Ketoolefins under the Conditions of Type II in Scheme 3

Entry	Starting Ether	R^1 =	R^2 =	Reaction Period (h)	Product[a]	Yield (%)[b]
1		$-CH_2OBn$	$-CH_2OBn$	(**30**) 6		(**32**) 89
2		$-CH_2OBn$	H	(**33**)[c] 18		(**40**) 63
3		$-CH_2OMe$	H	(**34**)[c] 12		(**41**) 68
4		Me	H	(**35**)[c] 21		(**42**) 53
5				(**36**) 18		(**43**) 65
6				(**37**) 14		(**44**) 70
7		$R = C_4H_9$		(**38**) 48		(**45**) 92
8		$C_{11}H_{23}$		(**39**) 24		(**46**) 88

[a] Olefinic stereochemistry is exclusively *E*. [b] Isolated yields, which are not necessarily optimized. When the product was hydroxy ketone, it was sometimes obtained as a mixture of the parent hydroxy ketone, cyclic hemiketal, and cyclic vinyl ether, depending upon subtle change in workup conditions. [c] These starting materials are a 1:1 mixture of diastereoisomers.

In conclusion, we reported a synthesis of dihydropyrans from benzyl ethers and a redox reaction of alkynyl ethers that yields ketoolefins, both catalyzed by a rhodium salt. Further investigations on these catalytic systems and synthetic application of their products, particularly by utilizing the versatile vinylsulfone moiety,[9] are in progress.

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Supporting Information Available: Experimental procedures and physical properties of products. This material is available free of charge via the Internet at http://pubs.acs.org.

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