Tetrahedron Letters xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

A Re_2O_7 catalyzed cycloetherification of monoallylic diols

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ARTICLE INFO

Article history:
Received 26 December 2016
Revised 17 January 2017
Accepted 20 January 2017
Available online xxxx

Keywords:
Cycloetherification
Rhenium catalyst
Monoallylic alcohol
Oxa-heterocycles
Lewis acid

ABSTRACT

A Re_2O_7 catalyzed cycloetherification of monoallylic diols is described. The reaction features short reaction time, mild reaction conditions and exclusive *E* selectivity. A wide range of monoallylic alcohols with alkyl or aryl substituents on olefin smoothly undergo ring closure to deliver corresponding oxa-heterocycles. The reaction is also operationally simple and not sensitive to air and moisture.

Oxa-heterocycles are privileged scaffold presented in natural products (Fig. 1, e.g. gambierol[1] and laurefurenyne[2]) and pharmaceutical molecules.[3] Therefore, enormous protocols for construction of oxa-heterocycles have been developed to enable the rapid and stereospecific access to such moiety.[3] In this regard, direct cycloetherification of monoallylic diols via nucleophilic substitution of allylic alcohol is a competent tool for synthesis of oxa-heterocycles due to the ready availability of starting materials and environmentally benign of this reaction (water as the only waste).[4–10] Additionally, it also provided a versatile handle (alkene) for further manipulations of the resulting oxa-heterocycles. Since the first Pd(0) catalyzed cycloetherification of monoallylic diols described by Stork,[4] extensive studies has been devoted to this stereospecific cycloetherification reactions, especially using Pd(II) catalyst.[5] Subsequent experimental observations and mechanistic studies revealed a "syn coordination, syn oxypalladation, and syn elimination" reaction pathway.[5d] However, other reaction pathways could not be totally ruled out, which depend on the substrate structure and reaction conditions.[5g] Despite of the easy availability of Pd catalysts, the high catalyst loading retards its synthetic applications.[5]

Other transition metals such as Au,[6] Ru[7] exhibit excellent efficiency on promoting diastereoselective or stereoselective cycloetherification of monoallylic diols. However, those catalysts suffer from high price and non-commercial availability. Lewis acid such as $FeCl_3$,[8a] $BF_3.OEt_2$[8b] are also capable of catalyzing this reaction, while those reactions are limited to narrow substrate scopes. Strong Brϕnsted acids (such as HCl,[9a] Amberlyst-15[9b]) have long been known to be efficient promoters for the dehydration of monoallylic alcohol. However, only tertiary or arene substituted alcohols are suitable for these reaction conditions. Recently, Hall and co-worker developed intramolecular oxy-cyclization of allylic alcohol by using boronic acid as mild catalyst.[10] More recently, Qu and coworkers found that intramolecular direct substitution of allylic alcohol by hydroxyl group could be realized in hot water.[11] However, both Hall and Qu's protocols need phenyl present on olefin carbon to generate the stable benzyl carbocation intermediate.

It's well documented that Re(VII)-oxo complexes are potent catalysts for the isomerization of allylic alcohols via concerted or anionic reaction pathway under very mild reaction conditions.[12] On the other hand, Re(VII)-oxo complexes also exhibit Lewis acid property, which have been used as effective promoters for acetalization, Prins cyclization and dienone-Phenol rearrangement.[13]

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http://dx.doi.org/10.1016/j.tetlet.2017.01.066
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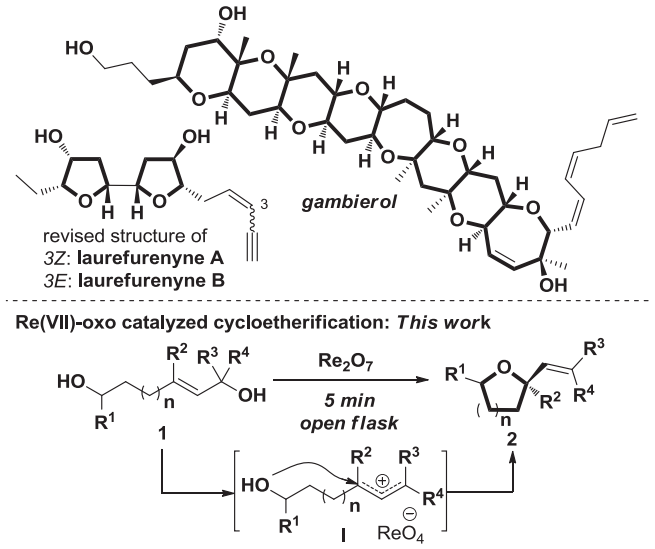


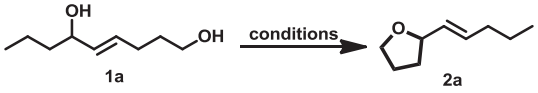
Fig. 1. Selected natural products incorporated with oxa-heterocycles and Re(VII)-oxo promoted cycloetherification of monoallylic diols.

Consequently, tandem allylic isomerization/nucleophilic cyclization catalyzed by Re(VII)-oxo has emerged as a novel strategy for constructing oxa-heterocycles in recent years.[14] As a continuation of our work on the Re(VII) chemistry,[13h,14d] we envisioned that when monoallylic diol is subjected to the action of Re_2O_7, an allyic carbocation intermediate **I** could be generated (Fig. 1), which would be intercepted by the appendage alcohol to produce 2-vinyl substituted oxa-heterocycles. Herein, we would like to report that Re_2O_7 catalyzes a very fast cycloetherification of monoallylic diols under mild reaction conditions.

Our studies commenced with the cycloetherification of diol **1a** under various V(V) or Re(VII)-oxo complexes based on the facts that those catalysts could efficiently produce allylic carbocation intermediate from allylic alcohol.[12a,12b] Initially, O = VSO_4, POVO and MTO were found to be ineffective for this reaction, which only resulted in full recovery of diol **1a** (Table 1 entries 2–4). To our delight, Ph_3SiO-ReO_3 and Re_2O_7 were both competent promoters for this reaction (Table 1, entries 5 and 6). It was also noteworthy that the reactions were completed in 5 min, producing vinyl tetrahydrofuran **2a** in excellent yields. As Re_2O_7 was commercially available, Re_2O_7 was selected as the optimal catalyst for this reaction. Subsequent screening of various solvents revealed that CH_2Cl_2 was the best reaction medium (Table 1, entries 7–12) and coordinated solvents such as ethyl acetate THF and CH_3CN only led to partial conversion of diol **1a** even after longer reaction time (Table 1, entries 10–12). Furthermore, catalyst loading could be reduced to 2.5 mol% without deteriorating the isolated yield and slowing down the reaction rate (Table 1, entries 14).

After establishing the optimal reaction conditions, the substrate scope was subsequently examined. Placing alkyl groups, electron-rich or electron-deficient aromatic substituents on C-1 of the allyl alcohol had no reverse effects on the reaction rate and led to the formation of cyclized products in very high yields (Table 2, 2a to 2j). This could be ascribed to the very high oxo-affinity of Re(VII)-oxo complex to allylic alcohol, enabling the facile formation of allylic carbocation intermediate. Gram scale synthesis of **2d** was also successively implemented to showcase the synthetic utility of this reaction. Substrate with inner allylic alcohol (Table 2, **1k**) was also reactive toward the reaction conditions, producing corresponding tetrahydrofuran **2k** in good yields. Next, the formation of tetrahydropyran ring via this protocol was investigated. Fast and clean reactions was also observed for cyclization of monoallylic diols **1l** to **1m**, producing tetrahydropyran **2l** to **2m** in good to excellent yields. Putting substituents on C-3 slightly reduced the yields, displaying that tetra-substituted carbon center could be constructed via this reaction (Table 2, 2m and 2n). Allylic alcohol with appendage secondary hydroxyl group also smoothly underwent cycloetherification, delivering tetrahydropyran **2o** in 88% yield with moderate diastereoselectivities (dr 4:1). It should be pointed out that only *E*-olefin was detected in all these reactions, suggesting a thermodynamically favored reaction pathway.

Table 1
Reaction condition optimization.[a]



Entry	Catalyst[d]	Solvent	*t*	**1** (%)[b]	Yield (%)[b]
1	–	CH_2Cl_2	2 h	100	0
2	O=VSO_4	CH_2Cl_2	2 h	100	0
3	POVO	CH_2Cl_2	2 h	100	0
4	MTO	CH_2Cl_2	2 h	100	0
5	Ph_3SiO-ReO_3	CH_2Cl_2	5 min	0	95
6	Re_2O_7	CH_2Cl_2	5 min	0	95
7	Re_2O_7	$CHCl_3$	5 min	0	87
8	Re_2O_7	Toluene	5 min	0	83
9	Re_2O_7	CH_2ClCH_2Cl	5 min	0	86
10	Re_2O_7	EtOAc	2 h	21	48[c]
11	Re_2O_7	THF	2 h	38	36[c]
12	Re_2O_7	CH_3CN	2 h	22	63[c]
13[e]	Re_2O_7	CH_2Cl_2	5 min	0	94
14[f]	Re_2O_7	CH_2Cl_2	5 min	0	95

[a] **1** (0.1 mmol) in 0.5 mL solvent was added to a solution of catalyst (x mol%) in 0.5 mL solvent at rt.
[b] Isolated yields.
[c] Determined by ^{1}H NMR using 1,4-dimethoxybenzene as inner standard.
[d] 10 mol% catalyst loading.
[e] 5 mol% catalyst loading.
[f] 2.5 mol% catalyst loading.

Please cite this article in press as: Wan X., et al. Tetrahedron Lett. (2017), http://dx.doi.org/10.1016/j.tetlet.2017.01.066