Tetrahedron Letters 53 (2012) 5064–5067

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

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

Preparation of enol ester epoxides and their ring-opening to α-silyloxyaldehydes

Gregory K. Friestad *, Gopeekrishnan Sreenilayam, Joseph C. Cannistra, Luke M. Slominski

Department of Chemistry, University of Iowa, Iowa City, IA 52242, USA

ARTICLE INFO

Article history:
Received 12 June 2012
Revised 28 June 2012
Accepted 29 June 2012
Available online 10 July 2012

Keywords:
Enol esters
Epoxides
Aldehydes
Oxidation

ABSTRACT

The Z-selective ruthenium-catalyzed addition of aromatic carboxylic acids to alkynes was followed by dioxirane epoxidation to furnish enol ester epoxides with cis configuration. Upon treatment of enol ester epoxides with *tert*-butyldimethylsilyl triflate in the presence of 2,6-lutidine, synthetically useful α-silyloxyaldehydes were obtained. This novel transformation was facilitated by microwave irradiation.

The preparation of α-hydroxyaldehyde derivatives is a common prerequisite to many asymmetric syntheses of 1,2-difunctional compounds.[1] Nucleophilic additions and olefination reactions involving the aldehyde function of such compounds afford 1,2-diols and allylic alcohols, respectively (Fig. 1a).

α-Silyloxyaldehydes are widely applied in synthesis,[2] yet the commonly employed methods for preparation of enantiopure α-silyloxyaldehydes (e.g., multistep differential protection and oxidation of 1,2-diols, or diazotization and partial reduction of α-amino acid derivatives) are often quite unwieldy due to the need for functional group differentiations and protecting group interchanges. For example, a six-step sequence from malic acid was used to access aldehyde **1**[2a] and an 11-step sequence was used to prepare 2-silyloxynonanal **2**[2b] (Fig. 1b). Thus, access to α-silyloxyaldehydes can be more cumbersome when the precursors are beyond the scope of naturally abundant α-amino acids or α-hydroxyacids.

Although kinetic resolution[3] and organocatalytic α-oxidation of aldehydes[4] have offered great advances in accessibility of terminal 1,2-difunctional compounds, subsequent functional group manipulation steps are still required in order to reach the α-silyloxy- or α-hydroxyaldehydes. Convenience and efficiency of the access to α-hydroxy carbonyl compounds warrant further improvement, and therefore new approaches to these deceptively simple building blocks continue to emerge.[5]

In the course of our prior work involving radical addition chemistry of α-silyloxyaldehyde hydrazones,[6] we had occasion to consider alternatives to the aforementioned routes, and hypothesized that oxidative transformations of enol derivatives might offer some potential for improvements in versatility and efficiency. Although α-hydroxyketones may be synthesized by dihydroxylation of enol ethers[7] or oxidation of enolates,[8] the similar methodology for aldehydes results in formation of water-soluble hydrates or 'polar unidentified materials.' [9] Unprotected α-hydroxyaldehydes also exhibit oligomerization and tautomerization to hydroxyketones.[10] An oxidative conversion of terminal enol derivatives into α-silyloxyaldehydes, circumventing the difficulties in handling unprotected α-hydroxyaldehydes, would be an attractive complement to existing preparative methods. Here we describe the development of a new route to α-silyloxyaldehydes based on this hypothesis.

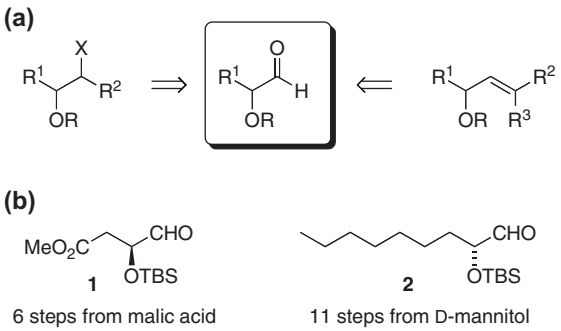


Figure 1. (a) Representative synthetic applications of α-hydroxyaldehyde derivatives. (b) Examples of α-silyloxyaldehyde preparations.

* Corresponding author. Tel.: +1 319 335 1364; fax: +1 319 335 1270.
E-mail address: gregory-friestad@uiowa.edu (G.K. Friestad).

0040-4039/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tetlet.2012.06.142

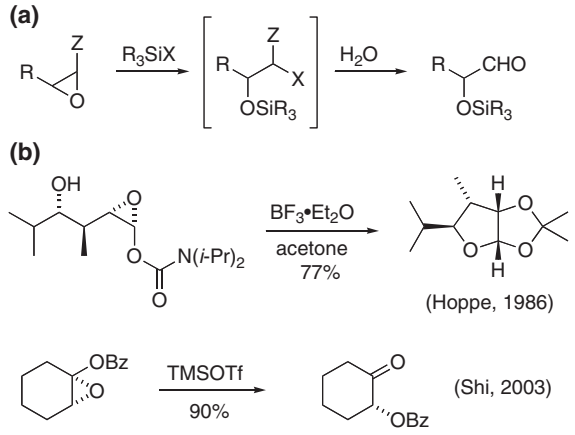
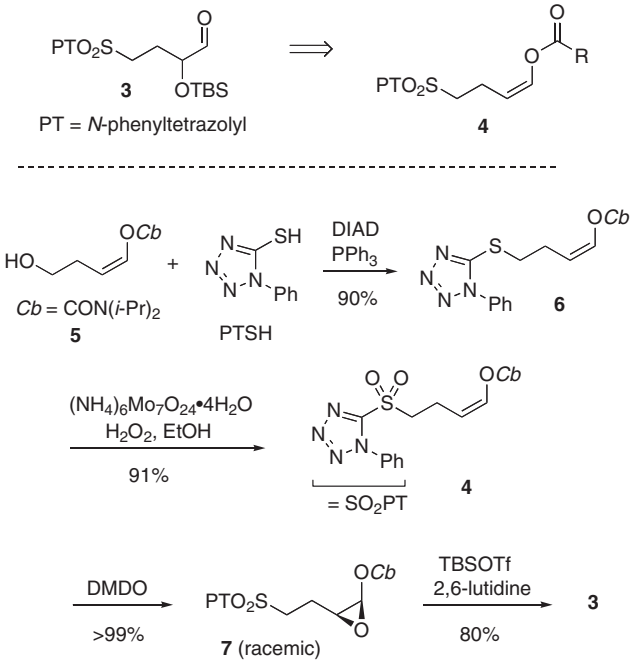


Figure 2. (a) Hypothesis for epoxide ring-opening route to α-silyloxyaldehydes (*Z* = carboxylate or other leaving group, *X* = OTf, Cl, etc.). (b) Relevant precedents involving ring-opening of enol ester epoxides.



Scheme 1. Proof of principle experiments for enol ester epoxide ring-opening to α-silyloxyaldehydes.

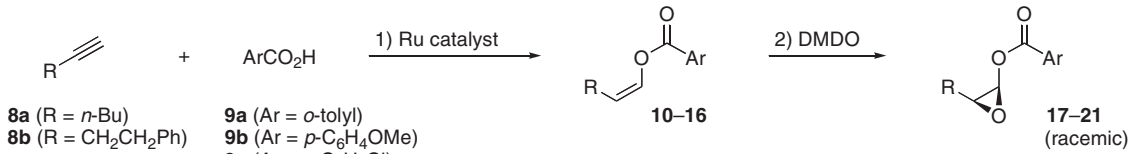
The novel reaction design in the proposed sequence is a silyl cation-induced ring opening of an epoxide derived from an enol derivative such as an enol ether or enol ester (Fig. 2a). In the presence of a silyl cation source, for example, a silyl triflate, the epoxide would be expected to be activated toward ring opening. We reasoned that, if the carboxylate group of an enol ester could serve dual roles as both a cation-stabilizing and leaving group, then the ring opening to an oxocarbenium ion could be followed by a simple hydrolysis to afford the desired α-silyloxyaldehyde. Precedent for such a reaction was sparse. Two examples are found in the work of Hoppe and Shi, each of whom described an isolated example (Fig. 2b).

The γ-sulfonyl α-silyloxyaldehyde **3** (Scheme 1) was needed in the pursuit of another synthetic objective, and presented an opportunity to test the feasibility of the above approach for preparing **3** from enol ester **4**. The *Z*-enol ester moiety was generated using the Hoppe allyl carbamate method,[11] homologating an allylic anion with formaldehyde to furnish the (*Z*)-enecarbamate **5** in 74% yield. Mitsunobu reaction with *N*-phenyltetrazolylthiol followed by oxidation of sulfide **6** provided the corresponding sulfone **4**. In the feasibility test, the enol ester was epoxidized with dimethyldioxirane (DMDO, generated in situ from oxone and acetone) to furnish chromatographically stable epoxide **7** in quantitative isolated yield. Upon treatment of **7** with TBSOTf and 2,6-lutidine at room temperature, aldehyde **3** was obtained in 80% yield, showing that the ring-opening pathway was indeed feasible.

With preparation of **3** establishing the proof of principle for the silyl cation-induced epoxide opening, we sought to link this key reaction to a convenient preparation of the requisite enol ester epoxides. Here, practical developments by Goossen in regio- and stereoselective Ru-catalyzed addition to alkynes[12] drew our attention; the ready availability of alkynes, either commercially or from a variety of precursors, is an important consideration for the scope of future applications.

Using Goossen's procedure, anti-Markovnikov addition of several substituted benzoic acids to 1-hexyne (**8a**, Table 1) or 4-phenyl-1-butyne (**8b**) occurred with 1 mol % loading of a Ru catalyst generated from commercial $[Ru(p\text{-cymene})Cl_2]_2$ and tri(*o*-chlorophenyl)phosphine in the presence of DMAP. The resulting enol esters were subjected to epoxidation with DMDO generated in situ under aqueous conditions, affording high yields of chromatographically stable epoxides **17**–**21**. The compatibility of these enol ester epoxides with the aqueous dioxirane conditions is notable, and suggests the potential for future application of catalytic asymmetric Shi epoxidation or related methodology.[13] The dimethylami-

Table 1
Preparation of enol ester epoxides[a]



Entry	R^1	Ar	Yield, enol ester	Yield, epoxide
1	*n*-Bu	*o*-Tolyl	93%, **10**	95%, **17**
2	*n*-Bu	*p*-Anisyl	80%, **11**	90%, **18**
3	*n*-Bu	$p\text{-}C_6H_4Cl$	55%, **12**	74%, **19**
4	*n*-Bu	$p\text{-}C_6H_4NMe_2$	72%, **13**	—[b]
5	CH_2CH_2Ph	*o*-Tolyl	44%, **14**	86%, **20**
6	CH_2CH_2Ph	*p*-Anisyl	80%, **15**	91%, **21**
7	CH_2CH_2Ph	$p\text{-}C_6H_4NMe_2$	75%, **16**	—[b]

[a] Conditions: (1) $((p\text{-cymene})RuCl_2)_2$, $(p\text{-}ClC_6H_4)_3P$, DMAP, 60 °C; (2) oxone, acetone, $NaHCO_3$, H_2O. For details, see endnotes.[15]
[b] A mixture of epoxides was obtained.