Pergamon

Tetrahedron Letters 41 (2000) 3829–3831

TETRAHEDRON
LETTERS

Lewis acid-catalyzed regiospecific opening of vinyl epoxides by alcohols

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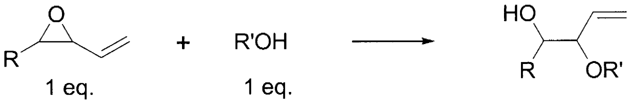
Received 17 February 2000; accepted 18 March 2000

Abstract

A Lewis acid-catalyzed, regiospecific opening of vinyl epoxides to β-hydroxy allyl-ethers was performed using equimolar quantities of both alcohols and oxiranes. $BF_3 \cdot Et_2O$ proved to be the most efficient catalyst for various substituted alcohols.

Keywords: vinyl epoxide; alcohol; ring-opening; Lewis acid.

In the course of our investigations of the synthesis of natural and non-natural *Annonaceous* acetogenins, we were interested in the nucleophilic ring-opening of vinyl epoxides with 1 molar equivalent of alcohol (Scheme 1).



Scheme 1.

Despite the rich literature on the chemistry of epoxide opening,[1] to the best of our knowledge there are few reports concerning ring-opening of vinyl epoxides by alcohols.[2–4] Nicolaou et al. demonstrated the CSA (camphorsulfonic acid)-catalyzed intramolecular ring-opening of vinyl epoxides.[2] Posner and Rogers reported the alumina-promoted opening of 1,3-cyclopentadiene monoxide with a large excess of allylic alcohol.[3] A palladium(II)-catalyzed ring-opening of vinyl epoxide with cyclic stannyl diether has also been described by Trost and Teneglia.[4] These last two examples are the only reported intermolecular reactions to date, and are limited to cyclic compounds[3] or require elaborate reagents.[4] Furthermore, general methods for the opening of non-vinylic epoxides with oxygen nucleophiles were

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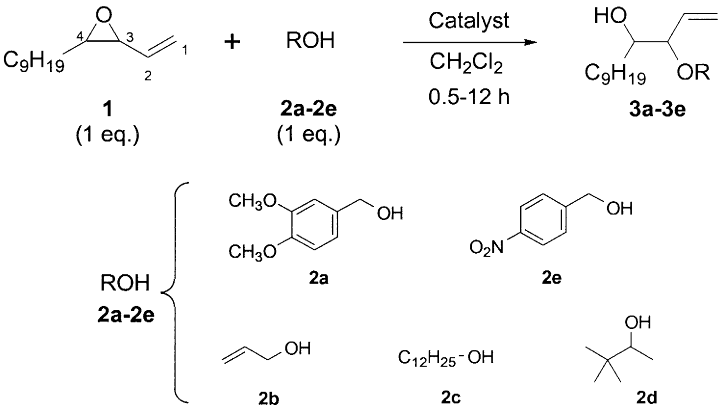
0040-4039/00/$ - see front matter © 2000 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(00)00496-2

usually performed with alcohol used in large excess or as solvent.[5] These features limit the synthetic utility of this reaction.

Here we present our results of a Lewis acid-mediated regiospecific opening of vinyl epoxides using equal amounts of alcohol and oxirane, leading to β-hydroxy allyl-ethers.

3,4-Epoxy-tridec-1-ene **1**, chosen as a model reagent, was prepared in a 60:40 *cis*:*trans* mixture from decylaldehyde and allyl arsonium ylide according to a known procedure.[6] Oxirane **1** was allowed to react with 1 equivalent of various types of alcohols (**2a**–**2e**) as shown in Scheme 2. Reactions were carried out at room temperature in methylene chloride (1 M) in the presence of different catalysts.



Scheme 2.

The ring-opening of **1** was first attempted with 3,4-dimethoxybenzyl alcohol **2a**. The reaction was very slow when using Nicolaou's intramolecular conditions (CSA 10% mol) and afforded **3a** in only a moderate yield (35% after 15 days). Similar results were obtained employing other organic acids such as PPTS (pyridinium-*p*-toluenesulfonate) or *p*TsOH. Either basic conditions (sodium alcoholate of **2a**) or $LiClO_4$ catalysis led to complete recovery of starting materials.

We then turned our attention to the use of Lewis acids. Catalytic amounts of $MgBr_2$, Et_2AlCl_2, Me_2AlCl_2, $Ti(OiPr)_4$ and $TiCl_2(OiPr)_2$ gave a rapid and complete degradation of the vinyl epoxide. Other Lewis acid catalysts proved successful (Table 1). Tin, titanium and zinc chlorides afforded the opened product **3a** in moderate yields (respectively, 15, 18 and 35%). Trimethylsilyl, tin, copper and iminium triflates generated the desired product in 55–73% yields. The use of $BF_3 \cdot Et_2O$ gave the best result: **3a** was isolated in a 76% yield using only 1% mol of catalyst after 30 min of stirring. $BF_3 \cdot Et_2O$ was selected (1% mol, 30 min) for the study of alcohols **2b**–**2e**. Yields were good with activated (**2b**, 75%), linear (**2c**, 73%) and hindered (**2d**, 70%) alcohols. Nucleophilic ring-opening even occurred in 52% yield with the deactivated alcohol **2e**.

The reaction yield was not significantly affected by changing the solvent (C_6H_6, Et_2O) and/or by varying the temperature (−78°C to reflux). In contrast, lowering the concentration from 1 to 0.1 M resulted in a lowering in yield (76 to 30% for **3a**). In all the reported examples the ring-opening reaction appeared to be regiospecific. Only nucleophilic attack at the C-3 position of the vinyl epoxide was observed (Scheme 2). It should be noted that β-hydroxy allyl-ethers were isolated as a 60:40 diastereomeric mixture similar to the *cis*:*trans* ratio of starting epoxide **1**. The only by-products resulted from the degradation of vinyl epoxide.[7]

In summary, we have presented the first preparative synthesis of β-hydroxy allyl-ethers by condensation of alcohols on a vinyl epoxide using equimolar quantities of both partners. The reaction was catalyzed by $BF_3 \cdot Et_2O$ (1% mol) in methylene chloride (1 M) at room temperature. The mild conditions

Table 1
Catalyzed ring-opening reaction of vinyl epoxide **1** (1 equiv.) with alcohols **2a**–**e** (1 equiv.)

ROH	Catalyst (mol%)	Yield[a] (%)	ROH	Catalyst (mol%)	Yield[a] (%)
2a	$SnCl_4$ (10)	15	**2a**	$Me_2N{=}CCl_2.OTf$ (2.5)	73
2a	$TiCl_4$ (10)	18	**2a**	$BF_3.Et_2O$ (1)	76
2a	$ZnCl_2$ (50)	35	**2b**	$BF_3.Et_2O$ (1)	75
2a	TMSOTf (10)	55	**2c**	$BF_3.Et_2O$ (1)	73
2a	$Sn(OTf)_2$ (10)	68	**2d**	$BF_3.Et_2O$ (1)	70
2a	$Cu(OTf)_2$ (10)	70	**2e**	$BF_3.Et_2O$ (1)	52

[a] products isolated by column chromatography

and easy work-up of this opening reaction allow its application to sensitive substrates as reported in the following paper,[8] where this methodology is used as a key step in the enantiospecific synthesis of (−)-muricatacin.

Experimental procedure: A 10% solution of $BF_3{\cdot}Et_2O$ (12 μL, 0.01 mmol) in CH_2Cl_2 was added dropwise to a mixture of **1** (1 mmol) and **2a**–**2e** (1 mmol) in CH_2Cl_2 (2 mL). The reaction was stirred for 30 min at room temperature and then concentrated under reduced pressure. The residue was purified by SiO_2 chromatography to yield β-hydroxy allyl-ether.

Acknowledgements

Financial support was provided in part by the Commissariat à l'Energie Atomique (fellowships for G.P. and C.B.).

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