

High valence vanadium complex promoted selective rearrangement of epoxides to aldehydes or ketones

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High valence vanadium complexes induce the selective ring opening of epoxides. The monosubstituted epoxides are isomerized with complete regioselectivity each forming a single carbonyl compound exclusively. Likewise a highly regioselective isomerization of 1,1-disubstituted or 1,1,2-trisubstituted epoxides was observed in all reactions.

Introduction

The high reactivity and ready availability of epoxides through a wide variety of synthetic methods make them versatile synthetic intermediates.¹ One of the most used reactions is their rearrangement to carbonyl compounds catalyzed by Lewis acids.² Two types of rearrangement are possible for substituted epoxides depending on the two possible migration patterns following Lewis acid promoted C–O bond cleavage. The rearrangement of the substituted epoxides with hydrogen or alkyl shift gives a ketone or an aldehyde, respectively.

Unfortunately low regioselectivity is observed in the rearrangement; the yield and the stereochemistry are strongly dependent on the epoxide structure. These problems are also observed, when epoxide opening inducers such as transition metals,³ or metalloporphyrins⁴ are used. The use of Pd(0) complexes⁵ and InCl₃⁶ has recently been reported to give highly regioselective ring opening reactions to benzylic aldehydes or ketones. In the present paper we describe the use of vanadium complex VO(OR)Cl₂ (R = Et, Prⁱ) as an alternative to those compounds to achieve a regioselective rearrangement. Such vanadium complexes have been reported by us in porphyrinic synthesis,⁷ and are versatile Lewis acids in organic media⁸ and can be used to generate radicals.⁹

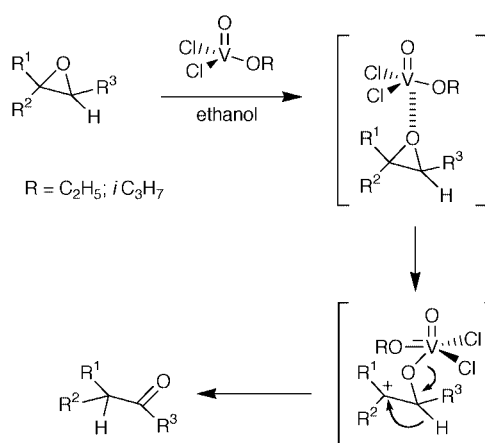
Results and discussion

The results from the rearrangement of various substituted epoxides are summarized in Table 1. Based on the observations of the chemo- and regioselectivity of the rearrangement products, the reaction mechanism should involve initial coordination between the vanadium and the oxygen from the epoxide, as in the mechanism proposed for the transposition of the epoxides by the action of the Lewis acids¹⁰ (Scheme 1).

Under the conditions of the experiments with the vanadium complex, addition to the C–O bond of monosubstituted and 1,1-disubstituted epoxides (entries 1–7) promoted their rupture, and hydrogen migration occurred selectively producing the corresponding aldehydes.

The lower stabilizing effect of the aryloxy group on the carbocation produced a slight decrease in the yield for aryloxy-methyl epoxides (entries 4, 5). This fact was also observed in monoalkyl and 1,1-dialkyl epoxides (entries 6,7), although in all the cases, only one rearrangement product was isolated. The absence of stabilizing effects on the intermediate carbocation can decrease the observed yield.

When the formation of two benzylic carbocations is possible, as with the 4,4'-disubstituted stilbene oxides (entries 8, 9), the opening is directed towards the formation of the more stable



Scheme 1

carbocation, which is determined by the substitution pattern of the aromatic rings. The greater migratory aptitude of hydrogen compared with the aryl substituent represents a significant difference from the epoxide openings catalyzed by Lewis acids. Very few similar examples of this alternative opening can be found in the literature.^{3,11} The exact reason for the selectivity achieved with VO(OR)Cl₂ is not very clear, however it could be related to the Lewis acid–transition metal dual character that these vanadium species show.¹²

On the other hand, in the 5-methyldec-5-ene oxide (entry 10) experiments a preferential isomerization occurred to yield 6-methyldecan-5-one *via* a hydride shift, while 2-butyl-2-methylhexanal, appeared as a secondary product as a consequence of alkyl migration. No differences in the regioselectivity of the opening in the obtained yield were observed with either of the vanadium species used: VO(OEt)Cl₂ or VO(OPrⁱ)Cl₂. In the same way, the mild conditions of the reaction allow compounds with other functional groups to be examined (*e.g.* CONH₂, H₃CO–, Cl–).

In order to compare our methodology to others described in the literature, we have studied the epoxide rearrangement with 1,2-epoxy-3-(1-naphthyl)propane as a model substrate (Table 2). Most significantly, VO(OR)Cl₂ is unique in pushing the reaction in one direction, providing the selective formation of aldehyde. With strong Lewis acids such as SbF₅ no stereoselectivity has been observed and a mixture of aldehyde and ketone (20:80) was produced. Only 1-(1-naphthyl)propan-2-one was obtained using Pd(0) complex as catalyst.

The reactions using VO(OR)Cl₂ are generally fast and high yielding, therefore, this methodology can be considered as an

Table 1 Rearrangement of epoxides with VO(OR)Cl₂ in ethanol

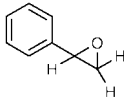
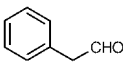
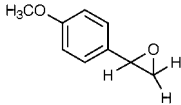
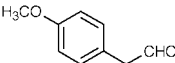
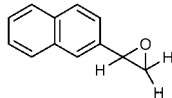
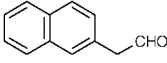
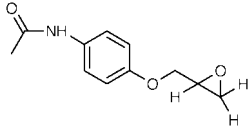
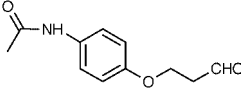
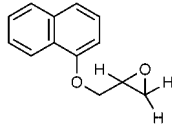
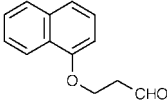
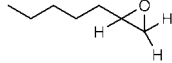
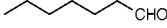
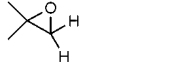

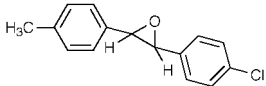
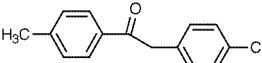
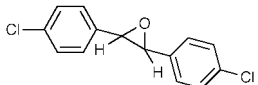
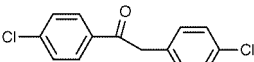
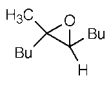

Entry	Epoxide	Time/h	Product	Yield (%)	Ref.
1		5		90	15
2		4		90	6
3		5		85	5b
4		4		70	
5		6		85	
6		7		60	2a
7		7		65	2a
8		6		75	
9		6		75	16
10		7		65	2a

Table 2 Epoxide opening reactions of 1,2-epoxy-3-(1-naphthoxy)propane using different rearrangement reagents

Reagent	Solvent	Conditions (T/°C, t/h)	Yield (%)	Ratio of aldehyde:ketone
VO(OEt)Cl ₂	Ethanol	25, 6	85	100:0
Pd(OAc) ₂ (PBu ₃) ₃	Benzene	80, 8	76	0:100
SbF ₅	Dichloromethane	-78, 5	50	20:80

alternative to the commonly described reactions using Lewis acid isomerization catalysts.

In these reactions the vanadium complex is not required in stoichiometric amounts, however an optimum amount is necessary.

In summary the epoxide openings promoted by high valence vanadium complexes provide a new synthetic access to carbonylic structures starting from epoxides, which complement the methods that already exist.

Experimental

All the reactions were performed under a nitrogen atmosphere. All solutions had been completely deoxygenated by passing

them through a column of reduced BTS catalyst (purchased from Fluka) and then dried by passage through a column of molecular sieves (4 Å). Liquid transfers were performed by syringe or cannula, and solid transfers were carried out under a stream of inert gas.

¹H and ¹³C NMR were recorded in CDCl₃ solution at 250 and 62.9 MHz respectively. IR spectra were measured on a Fourier Perkin-Elmer Paragon 1000 as neat films or KBr discs. Absorption bands are reported in cm⁻¹. CHN analyses were measured on a Perkin-Elmer 2400 autoanalyzer.

Preparation of vanadyl complexes

VO(OR)Cl₂ (R = Et, Prⁱ) was prepared by dropwise addition of

the alcohol (EtOH or PrⁱOH) to commercially available VOCl₃ in hexane, while N₂ was bubbled into the reaction mixture at room temperature. The vanadyl complexes were then distilled under reduced pressure: VO(OEt)Cl₂ 52–54 °C/2 mmHg; VO(OPrⁱ)Cl₂ 68–70 °C/4 mmHg.

Epoxide synthesis

The epoxides (Table 1, entries 1–3, 6, 7, 10) were obtained from olefins or carbonyl compounds by synthetic procedures previously described in the literature.^{2,4} The stilbene oxides (entries 8, 9) were obtained by oxidation of stilbene with MCPBA.¹³ Aryloxymethyl epoxides (entries 4, 5) were made by reaction of phenols with epichlorohydrin (1-chloro-2,3-epoxypropane).¹⁴ All epoxides were identified from their ¹H-NMR spectra and elemental analysis.

General procedure for epoxide rearrangement with vanadium complexes

A solution of the corresponding epoxide (0.5 mmol) in ethanol (5 ml) was treated with VO(OEt)Cl₂^{8a} (0.25 mmol) under N₂. The resulting solution was gently stirred at room temperature for 6 h. Then, small amounts of dilute aqueous HCl (NaCl saturated) were added to destroy the vanadium complex. The organic products were extracted with CH₂Cl₂ (3 × 50 ml). The combined organic layers were washed with water, dried over anhydrous Na₂SO₄ and the solvent evaporated under vacuum. The residue was purified by silica gel adsorption column chromatography.

This procedure was followed for the rearrangement of all the epoxides included in Table 1. Many of these products are known compounds and were easily characterized by comparison with authentic samples. Those that were unknown were identified by their spectral (IR, ¹H- and ¹³C-NMR) and analytical data. These data are presented below in order of the entries in Table 1.

3-[*p*-(Acetylamino)phenoxy]propanal (entry 4). IR (KBr) ν : 1720 cm⁻¹ (C=O). δ_{H} (CDCl₃, 250 MHz): 2.15 (s, 3H, CH₃), 2.40 (m, 2H, CH₂CHO), 3.90 (t, J = 7.2 Hz, 2H, CH₂-O), 6.85 (d, J = 8.5 Hz, 2H), 7.05 (s, 1H, NH), 7.39 (d, J = 8.5 Hz, 2H), 9.80 (t, 1H, CHO) ppm. δ_{C} (62.89 MHz, CDCl₃): 25.1 (CH₃), 46.3 (CH₂-CHO), 61.3 (CH₂-O-Ar), 115.0 (C2, C6), 121.9 (C3, C5), 132.7 (C4), 154.0 (C1), 167.6 (CONH), 190.8 (CHO) ppm (Found C, 63.66; H, 6.18; N, 6.72. C₁₁H₁₃NO₃ requires C, 63.8; H, 6.3; N, 6.8%).

3-(1-Naphthyl)oxypropanal (entry 5). IR (KBr) ν : 1720 cm⁻¹ (C=O). δ_{H} (CDCl₃, 250 MHz): 2.5 (m, 2H, CH₂CHO), 3.4 (t, J = 7.0 Hz, 2H, CH₂-O), 6.7 (d, J = 7.3 Hz, 1H), 7.3 (t, J = 7.3 Hz, 1H), 7.5 (m, 3H), 7.7 (m, 1H), 8.1 (m, 1H), 9.84 (t, 1H, CHO) ppm. δ_{C} (62.89 MHz, Cl₃CD): 46.3 (CH₂-CHO), 61.3 (CH₂-O-Ar), 105.0 (C2), 121.7 (C4), 126.5 (C3), 121.9 (C8), 125.6 (C9), 125.8 (C7), 126.9 (C6), 127.6 (C5), 134.0 (C10), 153.6 (C1), 190.8 (CHO) ppm (Found C, 77.66; H, 6.18. C₁₃H₁₂O₂ requires C, 77.98; H, 6.04%).

2-(4-Chlorophenyl)-1-(4-methylphenyl)ethan-1-one (entry 8). IR (KBr) ν : 1720 cm⁻¹ (C=O). δ_{H} (CDCl₃, 250 MHz): 2.41 (s, 3H, CH₃), 4.25 (s, 2H, CH₂), 7.25 (m, 6H), 7.90 (m, 2H) ppm. δ_{C} (62.89 MHz, Cl₃CD): 25.5 (CH₃), 56.3 (CH₂), 127.1 (C2, C6), 128.2 (C3', C5'), 129.7 (C3, C5), 130.0 (C2', C6'), 137.6 (C4), 137.8 (C1'), 138.1 (C1), 139.8 (C4), 197.0 (C=O) ppm (Found C, 73.5; H, 5.3. C₁₅H₁₃ClO requires C, 73.6; H, 5.3%).

General procedure for the rearrangement of epoxides with the Pd(0) complex

A suspension of Pd(OAc)₂ (70.2 mg, 0.31 mmol) in deoxygenated benzene (5 ml) was treated with PBu₃ (0.23 ml, 0.938

mmol) under N₂, whereupon formation of a yellow Pd(0) complex ensued. The solution was treated with 1,2-epoxy-3-(1-naphthyl)oxypropane (1.3 g, 6.5 mmol) and refluxed under N₂ for 8 h. The reaction mixture was then concentrated and purified on silica gel (hexane-CH₂Cl₂, 5:5), yielding the products given in Table 2. Analytical data are presented below.

1(1-Naphthyl)oxypropan-2-one. IR (KBr) ν : 1720 cm⁻¹ (C=O). δ_{H} (CDCl₃, 250 MHz): 2.3 (s, 3H, CH₃), 4.6 (s, 2H, CH₂), 6.6 (d, J = 73 Hz, 1H), 7.4 (t, J = 73 Hz, 1H), 7.5 (m, 3H), 7.8 (m, 1H), 8.3 (m, 1H) ppm. δ_{C} (62.89 MHz, CDCl₃): 26.7 (CH₃), 72.9 (CH₂), 104.7 (C2), 121.2 (C4), 121.8 (C8), 125.2 (C9), 125.5 (C7), 125.6 (C3), 126.6 (C6), 127.5 (C5), 134.5 (C10), 153.1 (C1), 205 (CHO) ppm (Found C, 77.72; H, 6.18. C₁₃H₁₂O₂ requires C, 77.98; H, 6.04%).

General procedure for the rearrangement of epoxides with a complex of SbF₅

To a solution of SbF₅ (1 mmol) in CH₂Cl₂ (10 ml) was added 1,2-epoxy-3-(1-naphthyl)oxypropane (0.01 g, 0.5 mmol) at -78 °C during 5 h. The solution was then poured into dilute HCl and extracted with CH₂Cl₂. The combined extracts were washed with saturated NaHCO₃ and dried over Na₂SO₄. Evaporation of solvents and purification of the residue through silica gel (hexane-ethyl acetate, 9:1), afforded the products shown in Table 2.

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