Vanadium-catalyzed Isomerization of Cyclopropanemethanols to Homoallylic Alcohols Involving C–C Bond Cleavage

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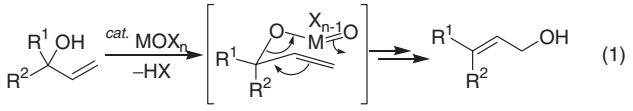
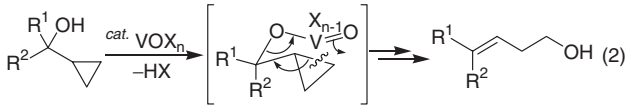
Some vanadium compounds work as effective catalysts for isomerization of cyclopropanemethanols to the corresponding homoallylic alcohols. This reaction may proceed via [3,3]sigmatropic rearrangement involving an oxovanadium cyclopropanemethanolate accompanied by the C–C bond cleavage.

The transformation of cyclopropanemethanols into homoallylic alcohols or halides is a useful reaction in organic synthesis and many methods for this reaction have long been developed.[1] The method has been applied for synthesis of some natural products such as vitamin D_2[2] and antitumor antibiotic, vicenistatin.[3] However, any catalytic methods using transition metal salts or their complexes have not been reported so far, in sharp contrast to the well-known transition metal (V,[4] Mo,[5] W,[6] Re[7])-catalyzed transposition of allylic alcohols via [3,3]sigmatropic rearrangement (Eq 1).[8]



(1)

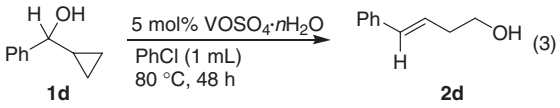
Recent reports of vanadium complex-catalyzed transposition of various propargylic and allenic alcohols[9] prompted us to investigate the isomerization of cyclopropanemethanols, a cyclopropane ring being considered to have a double bond nature, to the corresponding homoallylic alcohols (Eq 2) as one of our series of study on vanadium-catalyzed reactions.[10] A first successful example of such catalytic isomerization is described in a preliminary form.



(2)

First, treatment of cyclopropyl(diphenyl)methanol (**1a**) with 5 mol % $VO(acac)_2$ in toluene (0.5 mL; 0.4 M) at 80 °C for 48 h gave 4,4-diphenyl-3-buten-1-ol (**2a**) in 65% isolated yield and some unidentified mixtures as byproducts (Table 1, Entry 1). Among the solvents examined such as 1,2-dichloroethane, chlorobenzene, 1,4-dioxane, and acetonitrile, chlorobenzene was revealed to be the solvent of choice (Entries 1–5). When the reaction using other vanadium compounds such as $VOSO_4 \cdot nH_2O$ ($n = 3.3$), V_2O_5, $VO(tfac)_2$ (tfac = 1,1,1-trifluoroacetylacetonate), and $VO(hfac)_2$, (hfac = 1,1,1,5,5,5-hexafluoroacetylacetonate) as a catalyst was carried out in chlorobenzene, the highest yield of **2a** was obtained by use of $VOSO_4 \cdot nH_2O$ (Entries 6–9). The reaction under 0.2 M concentration improved the yield of **2a** (Entry 10).

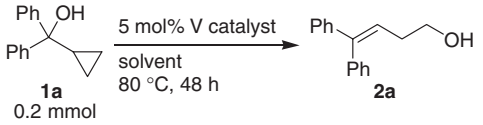
Next, the isomerization of other cyclopropanemethanols was examined under the condition of Entry 10 of Table 1. From cyclopropyl(phenyl)methanol (**1d**), the corresponding homoallylic alcohol **2d** was obtained in 33% isolated yield (Eq 3) in spite of high conversion of **1d**. As it was thought that the low yield was due to polymerization of the produced **2d**, the reaction was carried out in the presence of a polymerization inhibitor, 2,6-di-*tert*-butyl-*p*-cresol (butylhydroxytoluene: BHT). In this case, the isolated yield of **2d** was improved (Eq 3).



(3)

in the absence of inhibitor 33%
in the presence of BHT (0.02 mmol) 48%

Table 1. Vanadium-catalyzed isomerization of cyclopropanemethanol (**1a**) to homoallylic alcohol (**2a**)

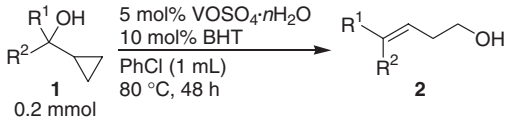


Entry	V Catalyst	Solvent/mL	Conversion /%	Yield /%[a]
1	$VO(acac)_2$	Toluene (0.5)	87	65
2	$VO(acac)_2$	$ClCH_2CH_2Cl$ (0.5)	91	69
3	$VO(acac)_2$	PhCl (0.5)	99	70
4	$VO(acac)_2$	1,4-dioxane (0.5)	99	56
5	$VO(acac)_2$	MeCN (0.5)	15	5
6	$VOSO_4 \cdot nH_2O$	PhCl (0.5)	93	81
7	V_2O_5	PhCl (0.5)	48	48
8	$VO(tfac)_2$[b]	PhCl (0.5)	99	57
9	$VO(hfac)_2$[c]	PhCl (0.5)	54	46
10	**$VOSO_4 \cdot nH_2O$**	**PhCl (1)**	**99**	**92**
11	$VOSO_4 \cdot nH_2O$	PhCl (2)	98	86

[a]Isolated yield based on **1a** employed. [b]tfac = 1,1,1-trifluoroacetylacetonate. [c]hfac = 1,1,1,5,5,5-hexafluoroacetylacetonate.

The results of vanadium-catalyzed isomerization of cyclopropanemethanols to the corresponding homoallylic alcohols in the presence of BHT are summarized in Table 2. Cyclopropanemethanol having an electron-donating methyl moiety on a phenyl ring (**1b**) was converted to **2b** in high yield (Entry 2), while treatment of cyclopropanemethanol having an electron-withdrawing chloro moiety on a phenyl ring (**1c**) gave **2c** in a slightly lower yield even for a longer reaction time (Entry 3). Alcohol **1d** was converted smoothly by the use of $VO(acac)_2$ as a catalyst (compare Entry 4 with Entry 5). Other alkyl- and aryl-substituted cyclopropanemethanols gave the corresponding homoallylic alcohols in good yield and selectivity (Entries 6–10). Cyclopropanemethanol having dialkyl substituent (**1i**) gave **2i** in low yield even when $VO(acac)_2$ was used as a catalyst

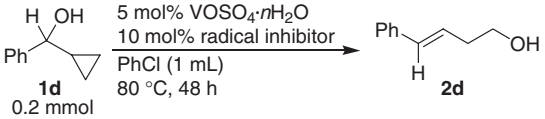
Table 2. Vanadium-catalyzed isomerization of various cyclopropanemethanols



Entry	Substrate **1**	Product **2**	Yield /%[a]	Major /Minor[b]
1	**1a** ($R^1 = R^2 =$ Ph)	**2a**	91	N.A.[c]
2	**1b** ($R^1 = R^2 =$ *p*-Tol)	**2b**	90	N.A.
3[d]	**1c** ($R^1 = R^2 =$ 4-ClC_6H_4)	**2c**	78	N.A.
4	**1d** (R^1 = Ph; R^2 = H)	**2d**	48	trans only
5[e]	**1d** (R^1 = Ph; R^2 = H)	**2d**	79	trans only
6	**1e** (R^1 = Ph; R^2 = Me)	**2e**	67	94/6
7[e]	**1e**	**2e**	70	93/7
8	**1f** (R^1 = Ph; R^2 = Et)	**2f**	66	83/17
9	**1g** (R^1 = Ph; $R^2 = {}^n$Bu)	**2g**	73	83/17
10[d]	**1h** (R^1 = Ph; R^2 = Bn)	**2h**	73	80/20
11	**1i** ($R^1 = R^2 = {}^n$Bu)	**2i**	17	N.A.
12[e]	**1i**	**2i**	40	N.A.

[a]Isolated yield based on **1** employed. [b]Determined by ^{1}H NMR. [c]Not applicable. [d]For 96 h. [e]$VO(acac)_2$ was used as a catalyst in place of $VOSO_4 \cdot nH_2O$.

Table 3. Effect of radical inhibitor



Entry	Radical inhibitor	Yield/%[a]
1	none	33
2	BHT	48
3	Galvinoxyl	55
4	*m*-Dinitrobenzene	56
5	1,1-Diphenyl-2-picrylhydrazyl	51

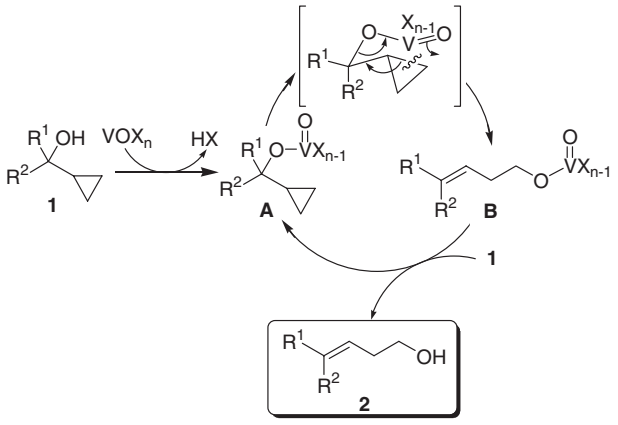
[a]Isolated yield based on **1d** employed.

(Entries 11 and 12).

In order to obtain some information about the reaction pathway, the effect of a radical inhibitor such as BHT, galvinoxyl, *m*-dinitrobenzene, and 1,1-diphenyl-2-picrylhydrazyl was investigated. As summarized in Table 3, the reaction was not prevented in the presence of any radical inhibitors, showing that this catalytic reaction does not proceed via radical pathway.

Although the details are not yet clear, we propose that the reaction may proceed via the pathway shown in Scheme 1 in analogy with the so-far known transposition of various alcohols: 1) an oxo metal complex reacts with cyclopropanemethanol to afford an oxo metal cyclopropanemethanolate (**A**), 2) the [3,3]sigmatropic rearrangement of this alcoholate accompanied by the C–C bond cleavage occurs to give an oxo metal homoallylic alcoholate (**B**) which then reacts with another cyclopropanemethanol to give the product homoallylic alcohol (**2**) and the oxo metal methanolate **A**.

In summary, we found a first transition metal complex-catalyzed isomerization of cyclopropanemethanols to the corresponding homoallylic alcohols. Further mechanistic studies as well as the reaction using other transition metals are in progress and will be published in due course.



Scheme 1.

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