

SYNTHESIS OF O-PROTECTED AZIDOHYDRINS CATALYZED BY TITANIUM
AND VANADIUM COMPLEXES.

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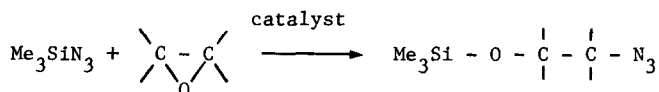
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Abstract : O-protected vicinal azidohydrins are obtained by titanium (or vanadium) complex catalyzed reaction of epoxides on Me_3SiN_3 via the formation of a transition metal-azide undergoing regio-selective insertion into the oxirane.

The role of early transition metal alkoxides such as $\text{Ti}(\text{O}i\text{-Pr})_4$ in epoxyalcohol chemistry has been recently reported.¹ On the other hand, some recent papers described the insertion of oxiranes into the silicon-halogen bond of Me_3SiX , $\text{X} = \text{Cl}$,² Br , I ³ but low regioselectivity is generally observed for the opening of unsymmetrical epoxides, especially in thermal uncatalyzed reactions. In a previous work one of us studied the regioselectivity of insertion of propylene oxide into the metal-chlorine bond of a wide variety of titanium and vanadium complexes and found that with Cp_2VCl_2 , for instance, the primary chloride was selectively obtained in 100 % yield.⁴

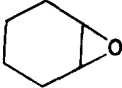

We now report the synthesis of O-protected vicinal azidohydrins by reaction of cyclohexene oxide and propylene oxide onto the silicon-azide bond of trimethylsilyl azide catalyzed by some titanium and vanadium complexes. The one pot reaction takes place under very mild conditions with 100 % yield and very good regioselectivity, 77 to 100 % of the primary azide, when starting from propylene oxide, while when starting from cyclohexene oxide only the trans isomer could be detected.

The general scheme is



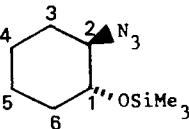
The reaction is run in THF with Me_3SiN_3 /oxirane/catalyst in 100/70/1 molar ratio. In a typical reaction 4.86 g of trimethylsilyl azide (42 mmol) and 1.71 g of propylene oxide (29.6 mmol) are added to a solution of 0.12 g of tetrakispropoxytitanium (0.42 mmol) in 7 ml of tetrahydrofuran, at room temperature. In a first step, the rate is very low (10 % yield after 2 days) then it becomes faster and after 6 days the conversion of propylene oxide is achieved.

Table I

Epoxide	Catalyst	Temp °C	Time ^a (days)	Selectivity
	Ti(Oi-Pr) ₄	R.T.	6	b
	Ti(Oi-Pr) ₂ (N ₃) ₂	R.T.	2	b
	Ti(Oi-Pr) ₄	R.T.	6	77 ^c
	Ti(Oi-Pr) ₄	45	4	73 ^c
	VO(Oi-Pr) ₃	75	8	92 ^c
	Cp ₂ VCl ₂	R.T.	25	100 ^c
	Cp ₂ VCl ₂	50	8	100 ^c
	Cp ₂ VCl ₂	70	5	100 ^c

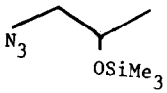
^a time corresponding to the complete disappearance of the epoxide followed by g.p.c.

^b



¹H n.m.r. δ ppm (in C₆D₆, 250 MHz) 0.28 (s,9H) 1.06 (m,2H) 1.44 (m,2H) 1.75 (m,2H) 3.03 (m,1H) 3.43 (m,1H).
 J Hz J₁₂ 8.8 ; J₁₆ 10.6 and 4.7 ; J₂₃ 11.4 and 4.7 to be compared with reference 8.
¹³C n.m.r. δ ppm (in C₆D₆, 62.9 MHz) 0.7(CH₃) 24.4-24.7(C4,C5) 31.0(C3) 35.3(C6) 67.5(C1) 75.8(C2) to be compared with reference 8.
 (the cis isomer could not be detected)
 i.r. ν_{asym.}(N₃) 2080 ; ν_{sym.}(N₃) 1295 cm⁻¹ (neat liquid) ; Eb₁ : 82°C.

^c % of the primary azide determined by g.p.c.⁷

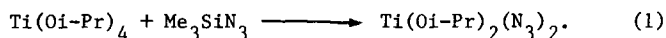


¹H n.m.r. δ ppm (in C₆D₆, 90 MHz) 0.13 (s,9H) 0.93 (d,3H) 2.73 (m,2H) 3.68 (m,1H).
 i.r. ν_{asym.}(N₃) 2070 ; ν_{sym.}(N₃) 1290 cm⁻¹ (neat liquid) ; Eb₁ : 27°C.

In the same experimental conditions, no reaction occurs in the absence of the transition metal complex.

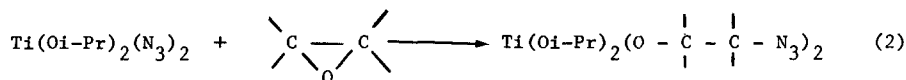
Table I summarized the experimental results obtained starting from cyclohexene oxide and propylene oxide using $\text{Ti}(\text{Oi-Pr})_4$, $\text{VO}(\text{Oi-Pr})_3$ and Cp_2VCl_2 as catalyst, from room temperature to 75°C .

The catalytic action of the titanium (or vanadium) complex can be explained on the basis of a sequence of elementary reactions, all of them being demonstrated by additional experiments on stoichiometric conditions. The formation of a transition metal azide as the first step is argued on the basis of the previously reported isolation of $\text{Ti}(\text{Oi-Pr})_2(\text{N}_3)_2$ and $\text{VO}(\text{Oi-Pr})(\text{N}_3)_2$ obtained by reacting $\text{Ti}(\text{Oi-Pr})_4$ and $\text{VO}(\text{Oi-Pr})_3$ respectively with Me_3SiN_3 during 5 days.⁵ The long initiation step of the catalytic process is then explained by :

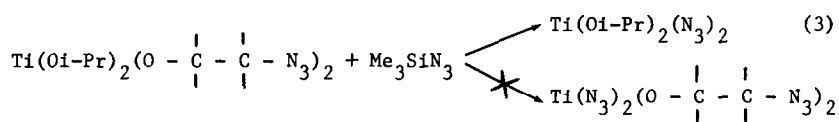


This initial stage can be avoided by directly using $\text{Ti}(\text{Oi-Pr})_2(\text{N}_3)_2$ as catalyst (see Table I).

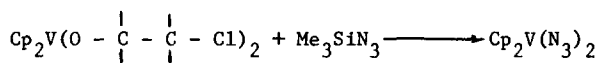
The second step is the insertion of the epoxide into the $\text{M}-\text{N}_3$ bond. As far as we know, reactions of this type have never been mentioned in the literature. They appear to take place within a few minutes on stoichiometric conditions⁶ giving for instance :



This azido-alkoxy group can be readily substituted by reaction with Me_3SiN_3 , owing to the electron withdrawing ability of the azido group and $\text{Ti}(\text{Oi-Pr})_2(\text{N}_3)_2$ is selectively obtained according to :

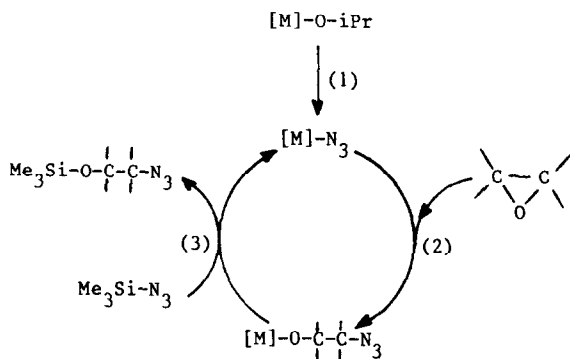


In the case of Cp_2VCl_2 , the formation of the intermediate azide $\text{Cp}_2\text{V}(\text{N}_3)_2$ cannot be obtained by direct substitution of the chlorine atoms on addition of Me_3SiN_3 ;⁵ it is generated by the insertion of the epoxide into the $\text{V}-\text{Cl}$ bond leading to a chloroalkoxy group (as previously reported⁴) which is then replaced by N_3 according to the scheme :



(Caution : explosive nature of $\text{Cp}_2\text{V}(\text{N}_3)_2$ in the solid state).

When the azide is formed, the catalytic sequence can take place according to the following scheme which is valuable in every case:



Obtention of the trans 0-trimethylsilyl vicinal azidoalcohol from cyclohexene oxide, together with the n.m.r. characterization ⁶ of the trans titanium homolog obtained on stoichiometric conditions (equation 2), suggests the mechanism for the insertion to involve a nucleophilic opening of the epoxide rather than a four center insertion into the carbon-oxygen bond in close similarity to previously reported results ^{2,9}.

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