Tetrahedron Letters, Vol.30, No.6, pp 739-742, 1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

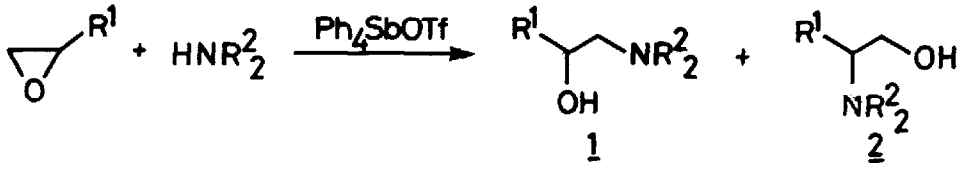
TETRAPHENYLSTIBONIUM TRIFLATE AS A REGIO- AND CHEMOSELECTIVE CATALYST IN THE REACTION OF OXIRANES WITH AMINES

Masahiro Fujiwara, Makoto Imada, Akio Baba* and Haruo Matsuda
Department of Applied Chemistry, Faculty of Engineering, Osaka University,
2-1 Yamadaoka, Suita, Osaka 565, Japan

Summary: Tetraphenylstibonium triflate catalytically promotes the nucleophilic addition of amines to oxiranes under mild conditions, giving the corresponding β-amino alcohols regio- and chemoselectively.

The synthesis of β-amino alcohols is a very important theme in both organic and medicinal chemistry,[1] and the addition of amines to oxiranes is a simple but useful methology. A satisfactory classical procedure involving the direct heating of oxiranes with amines has some significant limitations in the reaction with poorly nucleophilic amines.[2,3] These limitations recently could be overcome by transformation of amines into the corresponding metal amides.[4] In these cases, however, the use of equimolar amounts of moisture sensitive organometallic reagents and the hydrolysis of resulting metal alkoxides are both indispensable. Although it is thought that unactivated chromatographic alumina catalyst is one of the most effective procedure, the control of the reaction is considered to be difficult because of heterogeneous reaction.[5] Thus, catalytic, homogeneous and mild reaction of oxiranes with amines is desired.

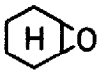
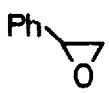
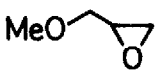
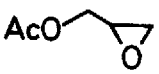
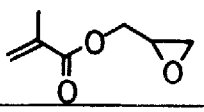
We have already revealed that pentavalent organoantimony compounds, in paticular tetraphenylstibonium iodide, show an inherent catalyst-activity for the cycloaddition of oxiranes with electrophilic heterocumulenes, promoting an unusual α-cleavage of oxiranes.[6] Meanwhile tetraphenylstibonium salts are anticipated to be very suitable for the cleavage of oxiranes. We now report a facile nucleophilic addition of amines to oxiranes in the presence of a catalytic amount of tetraphenylstibonium trifluoromethanesulfonate (tetraphenylstibonium triflate),[7] which was ascertained very effective (eq-1).



(eq-1)

A typical procedure is described for the reaction of cyclohexene oxide with diethylamine; under a nitrogen atomosphere, to a homogeneous

Table 1.[a]

run	oxirane	amine (HNR^2_2)	time (h)	yield (%)[f]	1 : 2
1		NR^2_2 = NEt_2	20	75[g]	
2[b]				70[g]	
3[c]				n.r.	
4[d]				n.r.	
5[e]				n.r.	
6		= NHPh		84[g]	
7[b]				36[g]	
8		= $NHCH_2Ph$		62[g]	
9		= 		71[g]	
10		= 		53[g]	
11		= NEt_2	6	100	100 : 0
12		= NHPh	5	100	100 : 00
13		= NEt_2	3	82	65 : 35
14		= NEt_2	3	80	100 : 0
15		= NEt_2	2	89	100 : 0
16		= NEt_2	2	85	100 : 0

[a]Oxirane/amine/cat.=3/3/0.3 mmol, 40 °C, solv. CH_2Cl_2 5 ml. [b]Ph_4SbI. [c]Ph_4SbCl. [d]Non catalyst. [e]MeOH solvent. [f]Determined by GLC. [g]Only trans-amino alcohols and no allylic alcohol was detected.

dichloromethane solution (5 ml) of Ph_4SbOTf (0.17 g, 0.3 mmol) and cyclohexene oxide (0.29 g, 3 mmol) was added diethylamine (0.22 g, 3 mmol) successively at room temperature, and then the mixture was stirred at 40 °C for 20 h. After cooling, volatiles were removed under reduced pressure and the resulting oil was subjected to silica gel column chromatography, producing trans-2-diethylaminocyclohexanol (eluted by chloroform).

Table 1 (runs 1-10) proves the efficiency of Ph_4SbOTf which allows the addition of low nucleophilic amines such as pyrrolidine and aniline under very mild conditions. A distinct advantage of Ph_4SbOTf to other catalysts is clear, since even Ph_4SbI had rather lower reactivity (run 2,7). Of interest is the

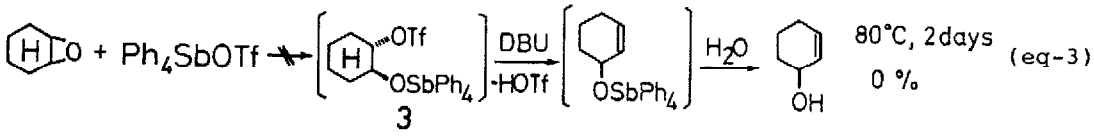
fact that a protic solvent, generally effective in reported direct reactions,[2] was not appropriate for our reaction. In this novel catalyst system, thus, the formation of amino alcohols could be accomplished under aprotic conditions.

Next, we attempted the reaction of terminal oxiranes, where the regiochemistry of oxirane cleavage is usually a significant problem. Tetraphenylstibonium triflate enhanced selective β-cleavage of oxiranes, affording 2-amino secondary alcohols **1** as summarized in Table 1 (runs 11-17). For example, in the reaction of methyloxirane with diethylamine 1-diethylamino-2-propanol was obtained exclusively (run 11).

High chemoselectivity was also observed as well as this regioselectivity. In general, metal amides are so basic that the selective formation of β-amino alcohols using them is not facile, for instance, the rearrangement of oxiranes to allylic alcohols happenes in almost cases.[8] However, as shown in Table 1, no allylic alcohol was obtained at all. Moreover, the functionalities such as acetyl group bearing active protones and polymerizable methacryl moiety could be tolelated to afford only the corresponding β-amino alcohols (run 15,16).

As mentioned, recent aminolysis reagents of oxiranes[4] are too moisture sensitive to be treated freely and resulting metal alkoxides need hydrolysis to give the corresponding amino alcohols. On the other hand, Ph_4SbOTf is a very handy compound due to chemical stability and no deliquescence, and is soluble easily in many organic solvents such as THF and dichloromethane. As this aminolysis is essentially allowed to be completed without hydrolysis of metal alkoxides, there is nothing to worry about the contamination with water in all steps including isolation.

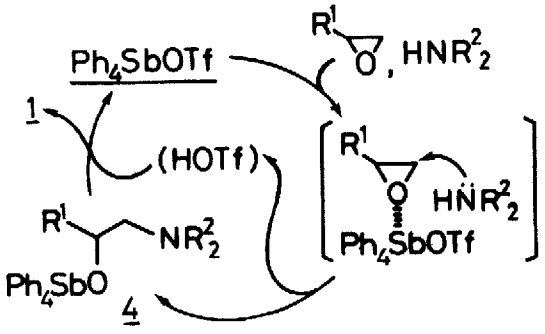
$$Ph_4SbOTf + HNR_2 \longrightarrow Ph_4SbNR_2 \qquad \text{(eq-2)}$$



3 (eq-3)

Although the details are not clear to date, we speculated two plausible mechanisms. The transition state illustrated in Scheme 1 is concerned in the first mechanism. Owing to a large ionic character of the Sb-O bond in Ph_4SbOTf,[7] the antimony atom coordinates to the oxygen atom in an oxirane to promote the nucleophilic attack of amines. The predominant attack at a less hindered carbon is reasonable. The resulting antimony alkoxide **4** reacts with trifluoromethanesulfonic acid to furnish an β-amino alcohol, and Ph_4SbOTf is regenerated. Another mechanism involves the formation of a pentavalent antimony amide from Ph_4SbOTf and an amine (eq-2). However, no facile reaction between them occurred, and there has been no report of successful formation of pentavalent antimony amides. Thus the former mechanism seems to be more plausible, but we can not exclude the later completely. It might be also

thinkable that an intermediate such as 3[9] reacted with amines to afford amino alcohols. Then we investigated the rearrangement of cyclohexene oxide using Ph_4SbOTf and DBU (eq-3), but there was no detectable allylic alcohol. Moreover, only trans amino alcohols were obtained as shown in Table 1. According to these results, the formation of 3 is ruled out.



Scheme 1

In conclusion, it was proved that Ph_4SbOTf is an effective regio- and chemoselective catalyst for the reaction of oxiranes and amines. Exact mechanism and the reaction with other nucleophiles such as alcohols are under investigation in our laboratory.

Acknowledgement: We are grateful to a support by a grant-in Aid for Scientific Research from the ministry of Education, Science and Culture.

References and Notes

1) See for example: Goodmann and Gilman's, "The Pharmacological Basis of Therapeutics", 6th ed.; L. S. Goodmann, A. Gilman, Eds, Mac Millan; New York, 1980.

2)(a) F. Möller, in "Methoden der Organischen Chemie (Houben-Weyl)", 4th ed., Vol. 11/1: E. Müller, Ed.; Thieme Verlog, Stuttgart, 1957, pp. 311-326. (b) M. Mousseron, J. Jullien and Y. Jolchime, Bull. Soc. Chim. Fr., 757 (1952). (c) J. A. Deyrup, C. L. Moyer, J. Org. Chem., **34**, 175 (1969). (d) P. A. Crooks, R. Szyndler, Chem. Ind. (London), 1111 (1973).

3) Cf, M. Freifelder and G. R. Stone, J. Org. Chem., **26**, 1477 (1961).

4)(a) L. E. Overman and L. A. Flippin, Tetrahedron Lett., **22**, 195 (1981). (b) M. C. Carre, J. P. Houmounou and P. Caubere, ibid., **26**, 3107 (1985). (c) A. Papini, A. Ricci, M. Taddei, G. Seconi and P. Dembech, J. Chem. Soc. Perkin Trans. I, 2261 (1984).

5) G. H. Posner and D. Z. Rogers, J. Am. Chem. Soc., **99**, 8208 (1977).

6)(a) A. Baba, M. Fujiwara and H. Matsuda, Tetrahodron Lett., **27**, 77 (1986). (b) M. Fujiwara, A. Baba and H. Matsuda, J. Heterocyclic Chem., in press.

7) R. Rüther, F. Huber and H. Preut, J. Organometal. Chem., **295**, 21 (1985).

8) See for example: C. L. Kissel and B. Rickborn, J. Org. Chem., **37**, 2060 (1972).

9) It is confirmed that the silyl analogues of 3 are obtained from oxiranes with trimethylsilyl triflate: R. Noyori, S. Murata and M. Suzuki, Tetrahedron, **37**, 3899 (1981).

(Received in Japan 12 November 1988)