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NUCLEOPHILIC CATALYSIS IN THE INSERTION OF SILICON HALIDES INTO OXIRANES: A SYNTHESIS OF O-PROTECTED VICINAL HALOHYDRINS

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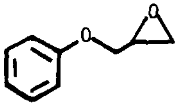
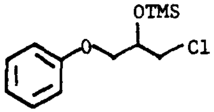
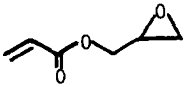
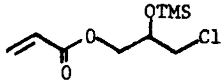
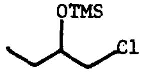
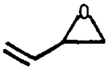
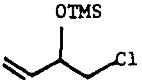
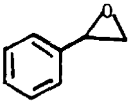
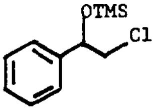
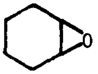
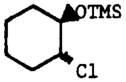
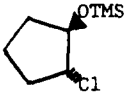
Abstract: Silicon halides in the presence of nucleophilic catalysts react with epoxides to form O-protected vicinal halohydrins with enhanced regioselectivity.

The thermal uncatalyzed insertion of silicon halides into oxiranes is well known in the literature.[1,2,3,4] However, due to the long reaction times, high temperatures often required in the reaction,[1e,1f] and the low observed regioselectivity for the opening of some unsymmetrical epoxides,[1j,1k,2] these insertions have received little use in synthesis. We now wish to report that the cleavage of oxiranes with silicon halides is subject to nucleophilic catalysis, allowing the regioselective formation of O-protected vicinal halohydrins under extremely mild conditions.[5]

A variety of catalysts are effective at promoting the insertion of silicon halides into oxiranes: the most effective in our hands are tetra-n-butylammonium chloride and triphenylphosphine.[6] In a typical reaction, one equivalent of halosilane is added to a stirred 10 wt% solution of the epoxide and 0.4 mole % catalyst in ethanol free chloroform with cooling. Table 1 shows several epoxide insertions performed in this manner, and in the case of entry 1 and 5 a comparison with the uncatalyzed reaction.

In all cases involving unsymmetrical epoxides, regioselective formation of the primary chloride is observed at low temperatures.[8] The regioselectivity is temperature dependent, the addition of chlorotrimethylsilane to styrene oxide at higher temperature (+5°) affords a 90:10 mixture of regioisomers. By comparison, the thermal insertion of chlorotrimethylsilane into styrene oxide has been reported to require 150 hr at 100° affording an 80:20 mixture of primary and secondary chlorides.[2] The insertion is influenced by the structure of the oxirane.

Table I: The Triphenylphosphine Catalyzed Insertion of Chlorotrimethylsilane into Epoxides.

Entry	Epoxide	Temp.	Cat.	Time	Yield[a]	Product
1		25° 25°	+ -	5 min 24 hr	99 23[b]	
2		25°	+	5 min	99	
3		-50°	+	45 min	99	
4		-50°	+	15 min	99	
5		25° +5° -50°	- + +	24 hr 5 min 15 min	0[b] 90[c] 99	
6		-50°	+	45 min	99	
7		25°	-	15 min	99	

a. Purity, yield and isomer ratios via ^{1}H, ^{13}C-NMR and glpc analysis.
b. The balance of material was composed of starting oxirane.
c. The balance of material was composed of the regio-isomer 2-chloro-2-phenyl-1-trimethyl-siloxyethane.

While the additions depicted by entries 1, 2, 5 and 6 do not occur in the absence of catalyst at room temperature, cyclopentene oxide rapidly affords the vicinal O-trimethylsilyl chlorohydrin[4] in an uncatalyzed process.

The formation of the primary chloride in the reactions with styrene oxide and butadiene monooxide and of trans O-trimethylsilyl vicinal chlorohydrins with cyclohexene and cyclopentene oxide 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.[3]

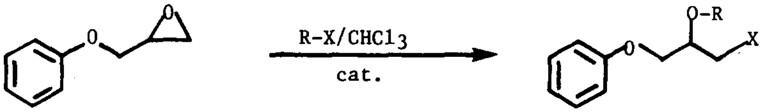


Table 2: The Catalyzed Insertion of Monohalosilanes into Phenyl Glycidyl Ether

X=	R=	Cat.	Condition	% Yield[a]
Cl	$(CH_3)_3Si$	$(C_6H_5)_3P$	0°/$CHCl_3$/5 min	99
Br	"	"	"	92
I	"	"	"	99[b]
Cl	$(CH_3)_2C_4H_9Si$	"	100°/Neat/20 hr	91
Cl	$(CH_3CH_2)_3Si$	(n-Bu)$_4N^+Cl^-$	60°/$CHCl_3$/22 hr	96
Cl	$(C_6H_5)_3Si$	"	60°/$CHCl_3$/48 hr	0

a. Isolated yields of 1-halo-2-O-silyl-3-phenoxypropanes.
b. Isolated as the vicinal iodohalohydrin.

The insertion reaction is general for trimethylsilyl halides. The catalyzed insertion of trimethylsilyl bromide and iodide into phenyl glycidyl ether (Table 2) regioselectively affords the corresponding primary halides at low temperature and in high yield. The reaction is also applicable to other substituted silicon halides to afford more hydrolytically stable vicinal halohydrin derivatives. The reaction of t-butyldimethylchlorosilane and triethylchlorosilane with phenyl glycidyl ether, while requiring higher temperatures and longer reaction times also afford the expected primary halohydrins in excellent yield.[10] In the absence of phosphine or alkylammonium chloride catalyst, no insertion was observed under these reaction parameters.

The addition of silyl halides[1] and pseudohalides (sulfides,[11] cyanides,[12] trifluoromethane-sulfonates,[13] selenides,[14] amines,[15] azides,[16] and amides[17]) to epoxides appears to be applicable not only to the case of silicon but other organometallic derivatives of the Group IVA as well.[18] The use of Lewis acid and nucleophilic catalysis to promote and/or modify reactivity in these reactions has now been observed in silyl selenides,[14] tin amines,[18c] and silyl halides.

Whether catalysis is a general property of the reaction of Group IVA halides and pseudohalides with oxiranes remains to be established.

References and Notes

(1) (a) Sauer, R. O. and Patnode, W. J. Amer. Chem. Soc., (1945), 67, 1548. (b) Mehrota, R. C. and Bajaj, P. J. Organometal. Chem., (1970), 22, 41. (c) Andrianov, K. A.; Sakolov, N. N.; Khrustaleva, E. N. and Yukin, L. N. Izv. Akad. Nauk. SSSR, Otd. Khim. Nauk., (1955), 531. (d) Shostakovskii, M. F.; Malinovskii, M. S.; Romantsevitch, M. K. and Kochkin, D. A. Ibid., (1956), 632. (e) Malinovskii, M. S.; Romantsevitch, M. K. J. Gen. Chem. (U.S.S.R.), (1957), 27, 1935. (f) Shigemi, Z. K. Nippon Kagaku Zasshi, (1960), 81, 1602. (g) Kraus, G. A. and Frazier, K. J. Org. Chem., (1980) 45 2579. (h) Sakurai, H.; Sasaki, K.; and Hosomi, A. Tet. Lett., (1980), 21, 2329. (i) Denis, J. N.; Magnane, R.; Van Eenoo, M.; and Krief, A. Nouveau J. Chim., (1979), 3, 705. (j) Denis, J. N. and Krief, A., Tet. Lett., (1981), 22, 1429. (k) Ditty, M. R. and Seidler, M. D. J. Org. Chem., (1981), 46, 1283.

(2) Ceder, O. and Hansson, B. Acta Chem. Scand., (1976), 30(B) 574.

(3) Torri, J. and Mousseron, M. M. C. R. Acad. Sci. Paris, (1973), 277, 1053.

(4) Barnier, J. P.; Garnier, B.; Girard, C.; Denis, J. M.; Salaun, J. and Conia, J. M. Tet. Lett., (1973), 1747.

(5) The formation of chlorohydrins from symmetrical olefins via the action of silyl hydroperoxide has recently been reported and may involve the addition of chlorotrimethylsilane to oxiranes; see Ho, T.-L. Synthetic Commun., (1979), 9, 37.

(6) Other catalysts showing some activity include $(n\text{-Bu})_4N^+Br$, $(n\text{-Bu})_4N^+I^-$, KCN·18-Crown-6, $(n\text{-Bu})_3P$, imidazole and $Et_3(C_6H_5CH_2)N^+Cl^-$. Lewis acid and protic acid catalysts are less effective, promoting product decompositionand mixtures of regio-isomers ($ZnBr_2$, $ZnCl_2$, $ZnCl_4$, and p-toluenesulfonic acid). Inactive catalysts include chlorocarbonyl-bis-(triphenylphosphine)rhodium, AIBN and dichloro-bis(triphenylphosphine)-palladium.

(7) All compounds reported were characterized by ^1H and ^{13}C-NMR, IR and precise mass. Criteria of purity were obtained by gas chromatography.

(8) Acid catalyzed addition of chloride ion to 1,2-epoxybutane and butadiene mono-oxide are non-regioselective, affording at 40° in water/dioxane, 86% and 14% of the primary chlorides, respectively; see Addy, J. K. and Parker, R. E. J. Chem. Soc., (1965), 644.

(9) The role of phosphines as catalysts is probably via formation of phosphonium chloride salts with trace quantities of HCl in the $CHCl_3$ or the chlorotrimethylsilane.

(10) The opposite regiochemical results have been suggested for the uncatalyzed addition of alkyl chlorosilanes to propylene oxide; see Shostakovskii, M. F.; Malinovskii, M. S.; Romantsevitch, M. K. and Kochkin, D. A. CA 51: 1026.

(11) Rokach, J.; Girard, Y.; Guindon, Y.; Alkinson, J. G.; Larue, M.; Young, R. N.; Masson, P. and Holme, G. Tet. Lett., (1980), 1485.

(12) Lidy, W. and Sundermeyer, W. Tet. Lett., (1973), 1449.

(13) Murata, S.; Suzuki, M.; Noyori, R. J. Amer. Chem. Soc., (1979), 101, 2738.

(14) Miyoshi, N.; Kondo, K.; Murai, S. and Sonoda, N. Chem. Lett., (1979), 909.

(15) Itoh, K.; Sakai, S. and Ishii, Y. J. Org. Chem., (1967), 32, 2210.

(16) Birkofer, L. and Kaiser, W. Ann., (1975), 266.

(17) Birkofer, L. and Dickopp, H. Chem. Ber., (1969), 102 14.

(18) (a) Yoshio, I. Asahi Garasu Kogyo Gijutsu Shorei-kai Kenkyu Hokoku, (1967), 13, 479; CA 69: 96843. (b) Bats, J.-P. and Moulines, J. Tet. Lett., (1976), 2249. (c) Tzschach, A. and Reiss, E. J. Organometal. Chem., (1967), 8, 255.

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