REGIOSPECIFIC PREPARATION OF 2-OXAZOLINES PROMOTED BY SILICON TETRAFLUORIDE

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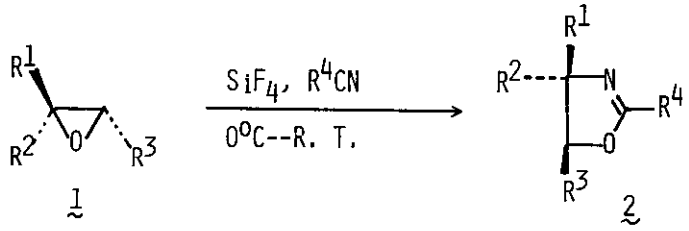
Abstract- Silicon tetrafluoride promotes reaction of oxiranes with nitriles to give 2-oxazolines in good yield.

2-Oxazolines have received considerable attentions as excellent synthetic intermediates, e. g., masked carboxylic acids, and possess diverse utilities for industrial applications.[1] A variety of synthetic procedures have been reported until now, and among them the reaction of epoxides with nitriles constitutes the most straightforward and attractive approach. However, the only procedure reported for that employs sulfuric acid at 0 °C --room temp as a promoter, and the yields of 2-oxazolines were generally less than 20 %.[2] We report herein that SiF_4[3] promotes reaction of oxiranes with nitriles effectively to form 2-oxazolines in good yields with high regioselectivities.



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Stirring a solution of styrene oxide (0.5 mmol) in acetonitrile (3 ml) under atmosphere of SiF_4 at room temp. for 1 h. gave 4-phenyl-2-oxazoline in 80 % yield.[4] A variety of 2-oxazolines was prepared under similar conditions, and Table 1 summarizes the results. As shown, 2-oxazolines were formed regiospecifically, i. e., the nitrogen atom was introduced into the more substituted carbons. The reaction proceeds generally in the nitrile as solvent under an excess of SiF_4. When a stoichiometric amount of nitrile was used, formation of a considerable amount of fluorohydrin[3] was observed. Although an electron-withdrawing group on the oxirane ring decreased the reactivity (run 10), the 1-cyano-2-oxazoline was formed in good yield under the more forcing conditions (at 80 °C). Furthermore, the present reaction has an important chemoselectivity: mono-substituted aliphatic oxiranes did not undergo 2-oxazoline formation but the starting materials were

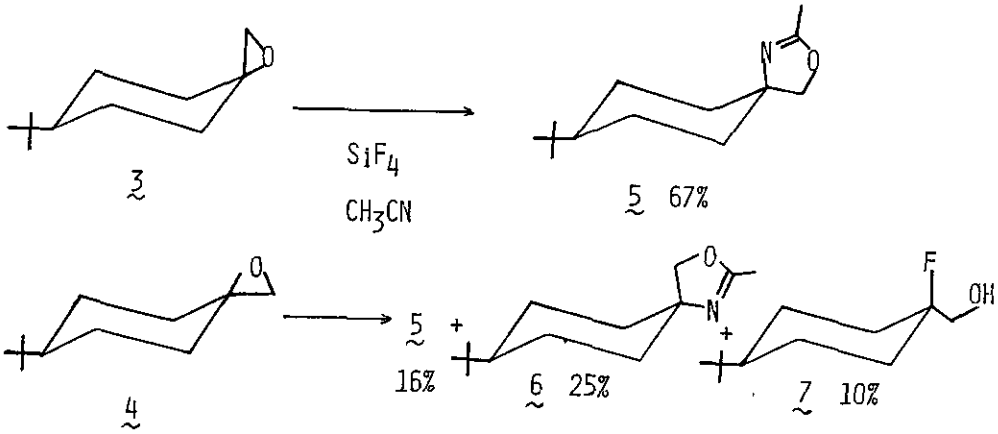
recovered almost unaffected.

Table 1. Preparation of 2-Oxazolines[a]

Run	R^1	R^2	R^3	R^4	Yield of 2 (%)[b]
1	Ph	H	H	CH_3	80
2	C_5H_{11}	C_5H_{11}	H	CH_3	65
3	C_5H_{11}	C_5H_{11}	H	C_2H_5	51
4	C_6H_{13}	CH_3	H	CH_3	52
5	—$(CH_2)_{11}$—		H	CH_3	45
6	CH_3	CH_3	$CH_2CH_2\overset{CH_3}{\underset{|}{C}}HCH_2CH_2OBn$	CH_3	61
7	CH_3	CH_3	$CH_2CH_2\overset{CH_3}{\underset{|}{C}}HCH_2CH_2OBn$	C_2H_5	63
8	CH_3	—$(CH_2)_4$—		CH_3	33
9	H	—$(CH_2)_{10}$—		CH_3	38
10[c]	C_5H_{11}	C_5H_{11}	CN	CH_3	74

[a]The reaction was carried out at 0 °C--room temp. for 1--12 h under an atmosphere of SiF_4. [b]All new compounds were fully characterized by nmr, ir, mass spectra, and/or combustion analyses, and in some cases by direct comparison with the authentic samples prepared by the reported method.[2] Yields refer to isolated materials. [c]The reaction was carried out at 80 °C.

The stereochemistry of the reaction was examined using 4-*t*-butylcyclohexane derivatives (3 and 4).[5] The oxirane (3) gave 5 exclusively in 67 % yield, whereas 4 gave a mixture of isomers together with fluorohydrin (7), indicating that an S_N1 process was involved in the case of 4 probably due to a substantial torsional strain on an attack from the equatorial side.[6]



The oxazoline formation exercised in the present study shows an extended utility of SiF_4 as selective Lewis acid.[7]

REFERENCES AND NOTES

1. J. A. Frump, Chem. Rev., 1971, 71, 483; A. I. Meyers and E D Mihelick, Angew. Chem. Int Ed. Engl., 1976, 15, 270; K. T. Potts in 'Comprehensive Heterocyclic Chemistry', vol. 5, ed. by A. R. Katritzky and C. W. Rees, Pergamon, Oxford 1984, pp. 112-166
2. R. Oda, M. Okano, S Tokiura, and F. Misumi, Bull. Chem. Soc. Jpn., 1962, 35, 1219.
3. SiF_4 promotes opening of oxiranes to form fluorohydrins; M. Shimizu and H. Yoshioka, Tetrahedron Lett., in press.
4. Reactions were most conveniently run in an ordinary glassware apparatus fitted with a balloon fillewd with SiF_4. After the completion of the reaction, an aqueous KF solution was added to the mixture, and normal workup followed by separation on SiO_2 TLC gave 2-oxazolines.
5. E. J. Corey and M. Chaykovsky, J. Am. Chem. Soc., 1965, 87, 1353.
6. The structures of 5, 6, and 7 were established based on their spectroscopic analysis. They afforded the following spectra: 5: ir(neat) 2950, 1670, 1475, 1440, 1385, 1235, 990, and 900 cm^{-1} ; pmr($CDCl_3$) δ 0.88(9H, s), 1.20-1.86(9H, m), 1.96(3H, s), and 3.80(2H, s). 6. ir(neat) 2950, 1680, 1450, 1380, 1360, 1225, 990, 895, and 750 cm^{-1} ; pmr($CDCl_3$) δ 0.86(9H, s), 1.16-1.88(9H, m), 1.96(3H, s), and 3.96(2H, s). 7: ir(neat) 3300, 2950, 1460, 1365, 1060, 880, and 735 cm^{-1} , pmr($CDCl_3$) δ 0.88(9H, s), 1.00-2.12(10H, m, including an OH proton), 3 54(2H, d, J=19.7 Hz); ^{19}Fnmr ($CDCl_3/CFCl_3$) -172 ppm Detailed explanation for the formation of fluorohydrin , see ref. 3.
7. SiF_4 is a good catalyst for glycosylation, see; S Hashimoto, M. Hayasi, and R. Noyori, Tetrahedron Lett., 1984, 25, 1379.

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