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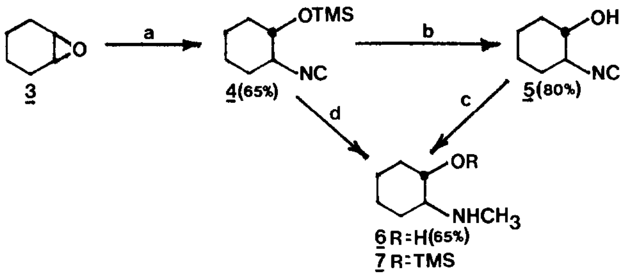
RING OPENING OF CYCLOHEXENE EPOXIDE WITH TRIMETHYLSILYL CYANIDE

Gary O. Spessard*, Allen R. Ritter[1], Dawn M. Johnson, and Anne M. Montgomery

Department of Chemistry
St. Olaf College
Northfield, MN 55057

Summary: Contrary to its reaction with epoxides in the presence of aluminum catalysts, trimethylsilyl cyanide reacts with cyclohexene epoxide to give 2-hydroxycyclohexyl isonitrile in the presence of $ZnCl_2$.

The reaction of epoxides with trimethylsilyl cyanide (TMSCN) to give trimethylsilyl ethers of 2-hydroxynitriles (1,2) was first reported by Lidy and Sundermeyer[2], and their results were confirmed in the very recent report of Mullis and Weber.[3] In contrast to their work, we have found[4] that cyclohexene epoxide (3) reacts with TMSCN to give the isonitrile (4)[5] and not the nitrile in the presence of $ZnCl_2$. The reaction was complete in 2 h at 60° when a $CHCl_3$ solution (*ca.* 10% w/w in either reactant) of TMSCN (*ca.* 2% molar excess) and 3 was allowed to react in the presence of a catalytic amount (*ca.* 100:1 substrate to catalyst mole ratio) of anhydrous $ZnCl_2$. When $ZnCl_2$ was absent under the same conditions, no reaction occurred after 4 h as indicated by glpc (6 ft. OV-17, column temp. 170°). The presence of the isonitrile group in 4 was confirmed by IR spectroscopy (ν = 2140 cm^{-1}) and through its conversion to the known *trans*-2-aminomethylcyclohexanol (6)[5,6] [bp 54-55° (0.5 mm), Lit.[6] bp 98° (10 mm); IR (thin film) ν = 3300, 3160, and 1065 cm^{-1}] *via* the hydroxyisonitrile (5)[5] [mp 59.5-60.5° (white glistening plates); IR (KBr) ν = 3380, 2150, and 1075 cm^{-1}]. Compound 6 could also be obtained directly from 4 by treatment with $LiAlH_4$/THF or Ra-Ni/H_2, but the alcohol was always obtained in the presence of significant amounts of the difficultly separable ether 7.



a) TMSCN/$CHCl_3$/$ZnCl_2$(tr)/60°; b) NH_4Cl/MeOH-H_2O (9:1 v/v)/65°; c) Ra-Ni/H_2 (2.5 atm)/EtOAc; d) Ra-Ni/H_2 (2.5 atm) or $LiAlH_4$/THF/25°

It is interesting to speculate on why aluminum Lewis acid catalysts direct attack by the carbon end of the ambident cyanide nucleophile to epoxide resulting in nitriles while zinc catalyzes only isonitrile formation. Mullis and Weber[3] suggest, as one possibility, the formation of 8 through ligand exchange between TMSCN and catalyst, and then attack by 8 on epoxide In terms of HSAB theory[7] the hard nitrogen end of CN^- complexes with hard acid Al^{3+} leaving the

Et_2AlNC 8 $ClZnCN$ 9

soft carbon end to attack the relatively soft, less-substituted carbon in the unsymmetrical epoxide[8] and thus yield nitrile. Reaction of TMSCN with the relatively soft Zn^{2+} in $ZnCl_2$ could, on the other hand, give 9 with the hard nitrogen end of the ligand now available to attack epoxide and yield isonitrile. The opposite regiochemistry with unsymmetrical epoxides would be expected with the zinc catalyst.

The reaction of TMSCN with 3 provides a convenient, relatively high-yield preparation of the synthetically versatile 2-hydroxycyclohexyl isonitrile.[9] Work is currently in progress to increase our knowledge of the synthetic utility and regiochemistry of epoxide ring opening with TMSCN and similar organosilicon reagents.

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References and Notes.

1. St. Olaf College Summer Chemistry Scholar.
2. Lidy, W.; Sundermeyer, W. *Tetrahedron Lett.* **1973**, 1449-1450.
3. Mullis, J.C.; Weber, W.P. *J. Org. Chem.* **1983**, *47*, 2873-2875.
4. Since we submitted our paper, another article on the same subject has appeared: Gassman, P.G.; Guggenheim, T.L. *J. Am. Chem. Soc.* **1982**, *104*, 5849-5850.
5. The spectral data (IR, NMR, MS) of all compounds were consistent with assigned structures, and elemental analyses of 4 and 5 were satisfactory. Yields reported in parentheses represent those for isolated, purified material.
6. Kay, J.B.; Robinson, J.B. *J. Chem. Soc.*, **1969**, 248-252.
7. Pearson, R.G.; Songstad, J. *J. Am. Chem. Soc.* **1967**, *89*, 1827-1836.
8. For a discussion of HSAB with several examples related to epoxide ring opening see Ho, T., "Hard and Soft Acids and Bases Principle in Organic Chemistry", Academic Press: New York, 1977.
9. The isonitrile group may be converted to a host of other functionalities; see Ugi, I. "Isonitrile Chemistry", Academic Press: New York, 1971.

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