esters were added at the top of the reactor at 1.2 cm^3/h (reactor volume ca. 30 cm^3), without a carrier gas flow. Products were collected in a trap maintained at dry ice temperature.

Product Analysis. Total conversion and the composition of the products were determined by GC using 30 m × 3.2 mm column packed with 23% SP-1700 on 80–100-mesh Chromosorb AAW and DB5 (60 m × 0.25 mm). The deuterium content of each butene isomer was determined using a HP5985A GC mass spectrometer equipped with a 30 m × 0.53 mm bonded Alteck FSOT RSL-160 capillary column and operated at 10 eV. The isotope composition of butenes were calculated from the area of *m/e* 56 and *m/e* 57. Peak *m/e* (M – 1) was very small (<2%); thus, the contribution of (M – 1) peak (*m/e* 56) for C_4H_7D should likewise be small so that it can be ignored. The deuterium isotope effect was calculated using the relative weight percent butenes from graphs 1 and 2 in the following equations:

$$\frac{k_h}{k_d} = \frac{(\text{1-butene})_H/(\textit{cis}\text{-2-butene} + \textit{trans}\text{-2-butene})_H}{(\text{1-butene})_D/(\textit{cis}\text{-2-butene} + \textit{trans}\text{-2-butene})_D}$$

for 1,1,1-trideuteriobutyl acetate and

$$\frac{k_h}{k_d} = \frac{(\textit{cis}\text{-2-butene})_H/(\textit{trans}\text{-2-butene} + \text{1-butene})_H}{(\textit{cis}\text{-2-butene})_D/(\textit{trans}\text{-2-butene} + \text{1-butene})_D}$$

for *d,l-erythro*-2-butyl-3-d_1 acetate.

Registry No. TB, 53716-61-3; EDB, 10277-59-5; SiO_2, 7631-86-9; tri-deuteriomethyl iodide, 865-50-9; propionaldehyde, 123-38-6; deuterium, 7782-39-0; *trans*-2,3-epoxybutane, 21490-63-1; 3-methyl-2-pentyl acetate, 34860-03-2; *erythro*-3-methyl-2-pentyl acetate, 24512-83-2; 2-octyl acetate, 2051-50-5; sec-butyl acetate, 105-46-4.

Regiospecific and Chemoselective Ring Opening of Epoxides with Trimethylsilyl Cyanide–Potassium Cyanide/18-Crown-6 Complex[1]

Mark B. Sassaman, G. K. Surya Prakash, and George A. Olah*

Donald P. and Katherine B. Loker Hydrocarbon Research Institute and Department of Chemistry, University of Southern California, Los Angeles, California 90089-1661

Received September 28, 1989

Trimethylsilyl cyanide with catalytic potassium cyanide/18-crown-6 complex opens epoxides regiospecifically to give 3-((trimethylsilyl)oxy) nitriles. The addition of cyanide occurs at the least substituted carbon. The reaction is chemoselective for monosubstituted epoxides due the participation of a pentavalent silicon species.

Introduction

Ring-opening reactions of epoxides with trimethylsilyl cyanide under Lewis acid catalysis have been the subject of considerable interest over the last 15 years. Trimethylsilyl cyanide is well known to exist in equilibrium with its isocyanide,[2] and due to this ambident nature, one may, by judicious choice of an appropriate catalyst, selectively obtain either β-((trimethylsilyl)oxy) nitriles[3] or isonitriles.[4] In general, harder Lewis acids (i.e., those containing aluminum) favor the formation of nitriles, while softer ones (containing zinc, tin, gallium, and palladium) favor isonitriles.[5] Control over the ambident nucleophilicity of trimethylsilyl cyanide as a function of the Lewis acid employed has been rationalized in terms of HSAB theory.[4b]

Regioselectivity in the formation of isonitriles invariably gives nucleophilic addition at the most highly substituted carbon,[6] suggesting that coordination of the Lewis acid to the epoxide oxygen and commensurate bond stretching toward a carbocation-like intermediate precedes nucleophilic attack. Attempts to delineate the course of regioselectivity in nitrile formation, however, have given conflicting results. Lidy and Sundermeyer found the cyano group added to the *most* highly substituted carbon in the reaction of trimethylsilyl cyanide with 2,2-dimethyloxirane and catalytic aluminum chloride.[3a] Mullis and Weber, on the other hand, reported that the same substrate underwent ring cleavage to give the cyano group at the *least* substituted carbon with either aluminum chloride or diethylaluminum chloride catalysis.[3b] Imi, Yanagihara, and Utimoto, also using 2,2-dimethyloxirane, obtained a mixture of nitrile (substitution at C-1), isonitrile (substitution at C-2), and a rearranged product with catalytic diethylaluminum chloride.[5] In their study, the isonitrile predominated. This group has also studied the effects of various Lewis acid catalysts, both hard and soft, on regioselectivity and on the ambident character of trimethylsilyl cyanide.[5]

Investigations of *anionically* catalyzed ring opening of epoxides with trimethylsilyl cyanide have, up to now, been left unexplored, although related carbonyl insertion reactions were studied by Evans as early as 1973.[7] Strong nucleophiles are well known to attack epoxides at the site offering the least steric hindrance. Thus, unambiguous ring opening to obtain regiochemically pure nitrile products by the use of an appropriate anionic catalyst was anticipated at the onset of this study. Our results, using potassium cyanide/18-crown-6 complex[7b] are described below. In addition to the expected regiospecific ring openings, under the conditions employed, we observed selective

---

[1] Synthetic Methods and Reactions. 144. For Part 143, see: Olah, G. A.; Weber, T.; Farooq, O. *Synthesis* **1989**, 569.

[2] (a) Seckar, J. A.; Thayer, J. S. *Inorg. Chem.* **1976**, *15*, 501. (b) Booth, M. R.; Frankiss, S. G. *Spectrochim. Acta* **1970**, *26A*, 859.

[3] (a) Lidy, W.; Sundermeyer, W. *Tetrahedron Lett.* **1973**, 1449. (b) Mullis, J. C.; Weber, W. P. *J. Org. Chem.* **1982**, *47*, 2873. (c) Caron, M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1557.

[4] (a) Gassman, P. G.; Guggenheim, T. L. *J. Am. Chem. Soc.* **1982**, *104*, 5849. (b) Spessard, G. O.; Ritter, A. R.; Johnson, D. M.; Montgomery, A. M. *Tetrahedron Lett.* **1983**, *24*, 655. (c) Gassman, P. G.; Gremban, R. S. *Tetrahedron Lett.* **1984**, *25*, 3259. (d) Gassman, P. G.; Haberman, L. M. *J. Org. Chem.* **1986**, *51*, 5010.

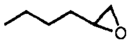
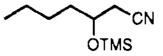
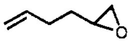
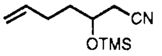
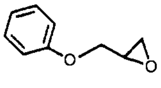
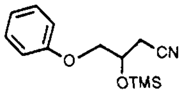
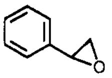
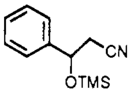
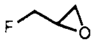
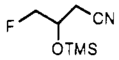
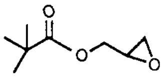
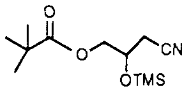
[5] Imi, I.; Yanagihara, N.; Utimoto, K. *J. Org. Chem.* **1987**, *52*, 1013 and references therein.

[6] The exception to this is propylene oxide, which gives ~1:1 mixtures of regioisomers with $Pd(CN)_2$, $SnCl_2$, and Me_3Ga (see ref 5).

[7] (a) Evans, D. A.; Truesdale, L. K. *Tetrahedron Lett.* **1973**, *49*, 4929. (b) Evans, D. A.; Truesdale, L. K.; Grimm, K. G.; Nesbitt, S. L. *J. Am. Chem. Soc.* **1977**, *99*, 5009.

0022-3263/90/1955-2016$02.50/0

Table I. 3-(Trimethylsiloxy) Nitriles

entry	epoxide	product	yield, %
1			66
2			80
3			85
4			74
5			74
6			82

cleavage of monosubstituted epoxides.

Results and Discussion

Regiospecific Ring Opening of Epoxides with Trimethylsilyl Cyanide–Potassium Cyanide/18-Crown-6 Complex. Monosubstituted epoxides, when heated to reflux temperature with 1.25 equiv of trimethylsilyl cyanide and 1 mol % potassium cyanide/18-crown-6 complex in the absence of solvent, undergo regiospecific ring opening at the nonsubstituted side, to yield 3-(trimethylsilyloxy) nitriles. The reactions are complete in 75 min or less, and the products are readily isolated by short path "flash" distillation directly from the reaction medium. Epoxides that are more highly substituted, either vicinally or geminally, remain unreactive under the same conditions. Yields of representative compounds are summarized in Table I.

All of the monosubstituted epoxides in the table gave products that were free from contamination by other regioisomers or isonitriles. Styrene oxide (entry 4), in addition to 3-phenyl-3-((trimethylsilyl)oxy)propanenitrile, unavoidably gave 8–10% of the dehydration product, *trans*-cinnamonitrile, as a contaminant. Under the same conditions, cyclohexene oxide, cyclopentene oxide, β-pinene oxide, 1,2-epoxy-2,3,3-trimethylbutane, and 1,2-epoxy-2,4,4-trimethylpentane did not react and could be recovered in greater than 90% yields. The reason seems to be that only sterically more accessible epoxides undergo the reaction (vide infra). The advantage of the new epoxide ring-opening reaction lies in using an acid-free system, the clean conversion to products, regiospecificity, and preference for monosubstituted substrates.

Mechanistic Aspects and the Nature of the Cyanide Reagent. While regiospecific ring cleavage at the least substituted carbon is in keeping with the expected outcome of nucleophilic attack, the preference for monosubstituted epoxides lies in the structure of the de fracto nucleophile. Dixon, Hertler, and co-workers have recently reported isolation and characterization of tetrabutylammonium dicyanotrimethylsiliconate, the first example of a pentacoordinate silicon with "all carbon bonded ligands".[8] The ^{13}C NMR spectrum reported for this compound is identical with that which we observe for the interaction of potassium cyanide/18-crown-6 complex with trimethylsilyl cyanide in CD_2Cl_2 for the regions corresponding to the silicon methyl and cyanide resonances. The results of our NMR studies have been reported elsewhere.[9]

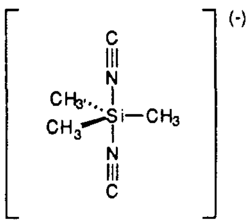


Figure 1.

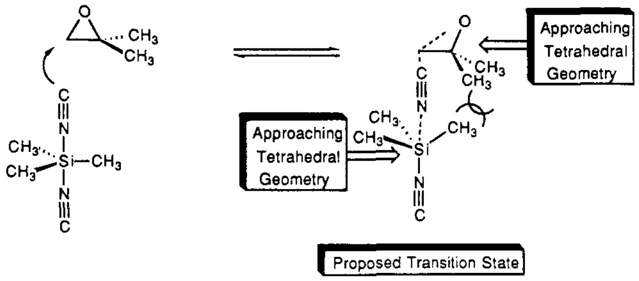


Figure 2.

Ab initio calculations have shown that pentavalent cyanosiliconates, in which the cyano groups are diaxial, are the lowest in energy.[8] For the two possible structures having D_{3h} symmetry, the N-bonded cyano groups are the most stable at the SCF level, while C-bonded are lower in energy at the MP-2 level (basis set 3). Our own semiempirical calculations, using AM1, which has recently been parametrized for silcon,[10] suggest that the dicyanotrimethylsiliconate possessing N-bonded cyano groups in D_{3h} symmetry is lower in energy. Thus, the most likely structure for the de facto nucleophile is the trigonal-bipyramidal structure shown in Figure 1.

The equilibrium constant (K) for the association of cyanide ion with trimethylsilyl cyanide at concentrations of 0.4 M in THF has been determined to be 2.3 M^{-1}.[8]

$$CN^- + Me_3SiCN \rightleftharpoons Me_3Si(CN)_2^-$$

Calculations using this value suggest that at concentrations typically employed in the ring-opening reactions, virtually all cyanide ion is associated as the pentavalent complex. Upon completion of the reaction, approximately 85% of the cyanide remains associated with excess trimethylsilyl cyanide. It then becomes clear why monosubstituted epoxides undergo the reaction, while those with higher degrees of substitution do not. In accordance with the Hammond Postulate, the geometries at the (late) transition state should resemble products. Thus, both the trigonal-bipyramidal silicon complex and the epoxide carbons begin to assume tetrahedral geometry as the cyanide group is transferred. The unfavorable steric interaction between the methyl groups attached to silicon and substituents on the epoxide prevent ring opening (see Figure 2). Apparently, one group on the epoxide still allows enough room for the approach of the nucleophile but two or more prohibit it.

Summary

Monosubstituted epoxides are regiospecifically ring opened by the reaction of trimethylsilyl cyanide and catalytic potassium cyanide/18-crown-6 complex to yield 3-((trimethylsilyl)oxy) nitriles. The addition of the cyano group

---

[8] Dixon, D. A.; Hertler, W. R.; Chase, D. B.; Farnham, W. B.; Davidson, F. *Inorg. Chem.* **1988**, *27*, 4012.

[9] Sassaman, M. B. Ph.D. Dissertation, University of Southern California, 1988, pp 62–65.

[10] Dewar, M. J. S.; Jie, C. *Organometallics* **1987**, *6*, 1486.

occurs on the nonsubstituted side of the epoxide. The chemoselectivity of mono- over disubstituted epoxides is attributable to the de facto nucleophile, dicyanotrimethylsiliconate, which provides appreciable steric interactions with substituents on the epoxide.

Experimental Section

Carbon-13 and proton NMR data were obtained on a Varian VXR-200 spectrometer. Infrared spectra were obtained on a Perkin-Elmer 1550 FT-IR. Mass spectra were obtained on a Finnegan MAT INCOS 50 GC/MS system. Microanalyses were performed by Oneida Research Services, Inc., Whitesboro, NY. Potassium cyanide/18-crown-6 complex was prepared by Evans' method.[7b] All other materials were purchased from Aldrich, Milwaukee, WI.

General Procedure for Ring Opening of Epoxides with Trimethylsilyl Cyanide–Potassium Cyanide/18-Crown-6. Trimethylsilyl cyanide (1.25g, 12.6 mmol) and the epoxide (10.0 mmol) are combined in a 10-mL round-bottom flask equipped with a magnetic stirring bar and efficient reflux condenser. To this is added potassium cyanide/18-crown-6 complex (0.04 g, 0.10 mmol), and the resulting bright yellow solution is refluxed under nitrogen for 75 min. Upon cooling, the reflux condenser is replaced by a short path distilling head, and the deep brown residue vacuum distilled. Pure 3-((trimethylsilyl)oxy) nitriles are obtained as colorless liquids.

3-((Trimethylsilyl)oxy)heptanenitrile (1): 66%; bp 92–94 °C (4.0 Torr); ^{13}C NMR ($CDCl_3$) δ 117.8, 68.3, 36.7, 27.3, 26.2, 22.4, 13.8, 0.0; ^{1}H NMR ($CDCl_3$) δ 3.9 (quint, 1 H), 2.4 (d, 2 H), 1.5 (m, 2 H), 1.3 (m, 4 H), 0.9 (t, 3 H), 0.1 (s, 9 H); IR (film) 2957, 2934, 2874, 2251, 1469, 1419, 1378, 1253, 1132, 1118, 1096, 1058, 1042, 953, 929, 842, 751, 687 cm^{-1}; MS *m/e* (relative intensity) 198 (M – H, 0.2), 184 (48), 159 (14), 143 (44), 128 (8), 115 (13), 98 (55), 73 (100), 59 (18). Anal. Calcd for $C_{10}H_{21}NOSi$: C, 60.24; H, 10.62; N, 7.02. Found: C, 60.27; H, 10.63; N, 6.87.

3-((Trimethylsilyl)oxy)hept-6-enenitrile (2): 80%; bp 88–90 °C (3.8 Torr); ^{13}C NMR ($CDCl_3$) δ 137.2, 117.68 115.2, 67.6, 36.0, 29.2, 26.2, 0.04; ^{1}H NMR ($CDCl_3$) δ 5.6–5.9 (m, 1 H), 4.9–5.1 (m, 2 H), 3.9 (t of t, 1 H), 2.4 (d, 2 H) 2.1 (m, 2 H), 1.6 (d of t, 2 H), 0.1 (s, 9 H); IR (film) 3492, 3079, 2957, 2361, 2251, 1643, 1418, 1370, 1253, 1100, 983, 964, 915, 842, 752, 688 cm^{-1}; MS *m/e* (relative intensity) 196 (M – H, 0.2), 182 (62), 141 (47), 113 (24), 98 (75), 73 (100), 67 (40). Anal. Calcd for $C_{10}H_{19}NOSi$: C, 60.86; H, 9.70; N, 7.10. Found: C, 60.76; H, 9.63; N, 7.06.

4-Phenoxy-3-((trimethylsilyl)oxy)butanenitrile (3): 85%; bp 158–160 °C (3.0 Torr); ^{13}C NMR ($CDCl_3$) δ 157.9, 129.5, 121.3, 117.3, 114.3, 70.0, 66.9, 23.7, 0.0; ^{1}H NMR ($CDCl_3$) δ 6.9–7.4 (m, 5 H), 4.4 (m, 1 H), 4.0 (m, 2 H), 2.7 (m, 2 H), 0.3 (s, 9 H); IR (film) 2957, 2251, 1601, 1589, 1498, 1472, 1458, 1416, 1302, 1248, 1174, 1125, 1080, 1052, 983, 932, 852, 754, 691 cm^{-1}; MS *m/e* (relative intensity) 249 (M$^+$, 10), 234 (25), 166 (10), 151 (85), 142 (18), 73 (100). Anal. Calc for $C_{13}H_{19}NOSi$: C, 62.61; H, 7.68; N, 5.62. Found: C, 63.28; H, 7.54; N, 5.64.

3-Phenyl-3-((trimethylsilyl)oxy)propanenitrile (4): 74% (contains 8–10% *trans*-cinnamonitrile; bp 119–121 °C (3.8 Torr); ^{13}C NMR ($CDCl_3$) δ 141.8, 128.5, 128.2, 125.4, 70.7, 29.5, –0.2; ^{1}H NMR ($CDCl_3$) δ 7.4 (m, 5 H), 5.0 (t, J = 6.5 Hz, 1 H), 2.7 (d, J = 6.5 Hz, 2 H), 0.2 (s, 9 H); IR (film, data for mixture) 3032, 2959, 2252, 2218, 1621, 1496, 1455, 1415, 1367, 1254, 1101, 1073, 1024, 935, 843, 752, 700 cm^{-1}; MS *m/e* (relative intensity) 218 (M – H, 0.4), 204 (12), 179 (35), 163 (9), 135 (10), 98 (59), 73 (100).

4-Fluoro-3-((trimethylsilyl)oxy)butanenitrile (5): 74%; bp 68–70 °C (1.5 Torr); ^{13}C NMR ($CDCl_3$) δ 116.8, 84.3 (d, $^{1}J_{C-F}$ = 174.6 Hz), 66.7 (d, $^{2}J_{C-F}$ = 22.1 Hz), 22.7 ($^{3}J_{C-F}$ = 6.0 Hz), –0.2; ^{1}H NMR ($CDCl_3$) δ 4.0–4.5 (m, 3 H), 2.5 (m, 2 H), 1.1 (s, 9 H), 0.1 (s, 9 H); IR (film) 2959, 2903, 2253, 1419, 1371, 1257, 1137, 1029, 995, 976, 947, 930, 868, 854, 844, 754, 690 cm^{-1}; MS *m/e* (relative intensity) 174 (M – H, 0.2), 160 (47), 142 (18), 132 (18), 118 (73), 105 (7), 98 (26), 77 (100), 73 (86). Anal. Calc for $C_7H_{14}FNOSi$: C, 47.97; H, 8.05; N, 7.99. Found: C, 48.02; H, 8.05; N, 7.90.

4-(Trimethylacetoxy)-3-((trimethylsilyl)oxy)butanenitrile (6): 82%; bp 122–124 °C (2.5 Torr); ^{13}C NMR ($CDCl_3$) δ 177.7, 117.0, 66.1, 38.6, 27.0, 23.8, –0.2; ^{1}H NMR ($CDCl_3$) δ 3.8–4.1 (m, 3 H), 2.5 (m, 2 H), 1.1 (s, 9 H), 0.1 (s, 9 H); IR (film) 2963, 2252, 1735, 1482, 1462, 1400, 1367, 1283, 1254, 1156, 1126, 1038, 1000, 931, 844, 752 cm^{-1}; MS *m/e* (relative intensity) 258 (M + H, 0.5), 242 (15), 188 (2), 173 (15), 159 (40), 142 (46), 117 (35), 85 (46), 73 (54), 57 (100). Anal. Calc for $C_{12}H_{23}NO_3Si$: C, 55.99; H, 9.00; N, 5.44. Found: C, 56.07; H, 8.98; N, 5.46.

Acknowledgment. Support by the National Science Foundation is gratefully acknowledged.