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Regiospecificity of Reactions of Epoxides and Oxetanes with Trimethylsilyl Cyanide

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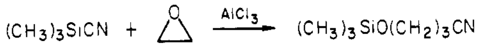
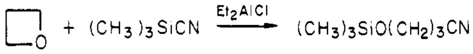
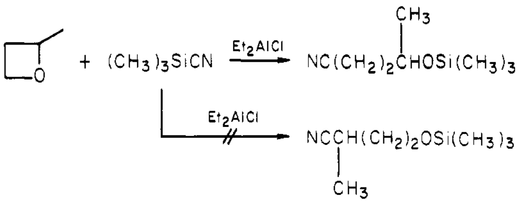
Lewis acid catalyzed reactions of trimethylsilyl cyanide with epoxides yield 3-[(trimethylsilyl)oxy]propionitriles, while similar reactions with oxetanes give 4-[(trimethylsilyl)oxy]butyronitriles. The regiospecificity of these reactions has been examined.

Epoxides have been reported to react with trimethylsilyl cyanide under the influence of aluminum chloride catalysis to yield 3-[(trimethylsilyl)oxy]propionitriles.[1] Similarly, we have found that oxetanes react with trimethylsilyl cyanide in the presence of a catalytic amount of diethylaluminum chloride to yield 4-[(trimethylsilyl)oxy]butyronitriles. Diethylaluminum chloride was utilized in place of aluminum chloride to eliminate the possibility that hydrochloric acid, a usual contaminant of aluminum chloride, was in fact the catalytic species. No reaction occurred in the absence of Lewis acid catalyst. This was not surprising since the strain energy of epoxides and oxetanes (~25 kcal/mol) is approximately equal.[2] Thus oxetane and 3,3-dimethyloxetane reacted with trimethylsilyl cyanide to yield respectively 4-[(trimethylsilyl)oxy]butyronitrile (100%) and 3,3-dimethyl-4-[(trimethylsilyl)oxy]butyronitrile (86%). 2-Methyloxetane, however, reacted with trimethylsilyl cyanide to yield 4-methyl-4-[(trimethylsilyl)oxy]butyronitrile (47%) rather than the anticipated 2-methyl-4-[(trimethylsilyl)oxy]butyronitrile. This result was unexpected since trimethylsilyl cyanide has been reported to react with isobutylene oxide to give 2,2-dimethyl-3-[(trimethylsilyl)oxy]propionitrile in which the nitrile has become bonded to the most rather than the least substituted carbon of isobutylene oxide.[1]

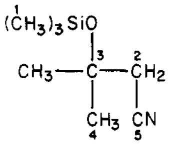
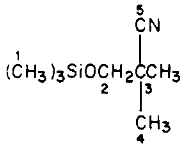




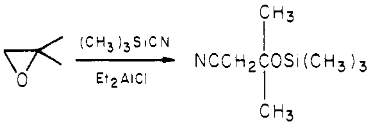


To clarify this apparent discrepancy we have reexamined the reaction of trimethylsilyl cyanide with isobutylene oxide with both aluminum chloride and diethylaluminum chloride catalysts. In both cases we found that the product obtained is actually 3-methyl-3-[(trimethylsilyl)oxy]butyronitrile (52%). Comparison of observed ^{13}C NMR chemical shifts with those calculated for the two possible isomeric products clearly favors 3-methyl-3-[(trimethylsilyl)oxy]butyronitrile rather than 2,2-dimethyl-3-[(trimethylsilyl)oxy]propionitrile[12] (see Table I).

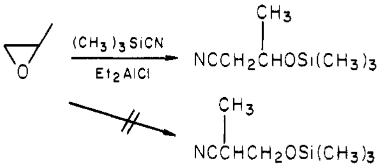
Table I. Comparison of Observed and Calculated ^{13}C NMR Chemical Shifts (δ)[12]

carbon	obsd	calculated for	
			
1	(q) 3.215	nc[a]	nc
2	(t) 34.592	32.4	84.4
3	(s) 71.899	75.9	30.9
4	(q) 30.103	25.4	22.4
5	(s) 117.400	nc	nc

[a] Not calculated.



Trimethylsilyl cyanide also reacted with propylene oxide under the influence of diethylaluminum chloride to give 3-methyl-3-[(trimethylsilyl)oxy]propionitrile (83%) rather than 2-methyl-2-[(trimethylsilyl)oxy]propionitrile.



These results are consistent with the following mechanistic hypothesis. A complex is initially formed between the Lewis acid and the oxygen of the strained ether. Ring opening may then occur via a six-membered-ring transition state in which nucleophilic attack by the carbon of the isocyanide form of trimethylsilyl cyanide occurs on the less substituted α-carbon of the oxetane–Lewis acid complex simultaneously with chloride attack on silicon. Trimethylsilyl cyanide is well-known to exist as an equilibrium mixture of nitrile and isocyanide forms.[3,4] Exchange of oxygen and chloride between silicon and aluminum then gives the product and regenerates the catalyst.

On the other hand, we have found that diethylaluminum chloride reacts with trimethylsilyl cyanide to yield trimethylchlorosilane and diethylaluminum cyanide. Fur-

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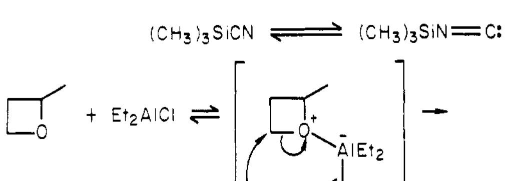
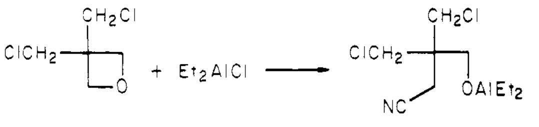
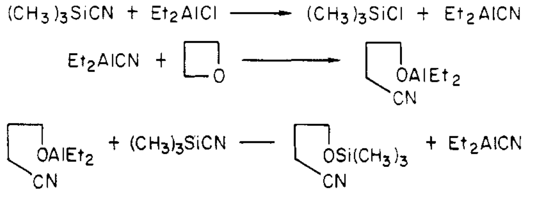


ther, ring opening of an oxetane by diethylaluminum cyanide has been observed.[5] These facts suggest an alternative mechanistic possibility. Initial reaction of trimethylsilyl cyanide with a catalytic amount of diethylaluminum chloride gives diethylaluminum cyanide and trimethylchlorosilane. Diethylaluminum cyanide then reacts with the oxetane to yield ring-opened product. Finally, exchange between additional trimethylsilyl cyanide and the diethylaluminum alkoxide serves to regenerate diethylaluminum cyanide and give the product. Our results do not permit us to distinguish between these two mechanistic possibilities.





In conclusion, these results demonstrate that both epoxides and oxetanes react with trimethylsilyl cyanide under Lewis acid catalysis analogously to yield ring-opened products in which the nitrile becomes bonded to the less substituted α-carbon of the strained ether.

Experimental Section

All ^{13}C and ^{1}H NMR spectra were recorded on a Varian XL-100 spectrometer operating in the FT mode, using chloroform-d_1 as solvent and chloroform as internal reference standard. For ^{1}H spectra, 1% solutions were used, while for ^{13}C spectra at least 10% solutions were needed. ^{13}C spectra were run with broad-band proton decoupling (A) or with off-resonance decoupling (B) to determine the multiplicity. IR spectra were recorded as neat samples on sodium chloride plates, using a Perkin-Elmer 281 spectrometer. Low-resolution mass spectra were determined on a Hewlett-Packard 5985 GC/MS instrument operating in the electron-impact mode with an ionizing voltage of 70 eV. A 5 ft × $^1/_8$ in. 3% OV-I on Chromosorb W 60/80 mesh column was used in the GC. Samples of all compounds for spectral analysis were purified by preparative vapor-phase chromatography on a Hewlett-Packard F&M 700 instrument using a 25 ft × 0.25 in. copper column packed with 20% SE-30 on Chromosorb W 60/80 mesh. Yields are based on the quantity of trimethylsilyl cyanide utilized, which was the limiting reagent in all cases. Elemental analysis was performed by Galbraith Laboratories, Knoxville, TN. All reaction mixtures were kept under an inert atmosphere of nitrogen. They were stirred with a Teflon- or glass-covered magnetic stirring bar. Yields were determined by GLC, using phenyltrimethylsilane as an internal standard unless otherwise stated.

Trimethylsilyl cyanide, propylene oxide, 2-methyloxetane, 3,3-dimethyloxetane, and oxetane were obtained from Aldrich. These ethers were dried over activated 4-Å molecular sieves prior to use. Ethylaluminum dichloride and diethylaluminum chloride were obtained from Alfa as 25% solutions in hexane. Most of the starting materials and products are known compounds. In those cases where complete spectral data have not been previously recorded this information has been included.

Isobutylene oxide was prepared from 1-bromo-2-methyl-2-propanol by reaction with aqueous potassium hydroxide.[6] 1-Bromo-2-methyl-2-propanol was prepared by passing isobutylene (Matheson) through an aqueous solution of bromine and potassium bromide.[7]

Reaction of 3,3-Dimethyloxetane with Trimethylsilyl Cyanide. In a dry 2-mL two-necked round-bottom flask equipped with a reflux condenser was placed a mixture of 25 μL of diethylaluminum chloride solution and 0.246 g (4.48 mmol, 330 μL) of trimethylsilyl cyanide. To this was added, over a period of 1 h, 0.288 g (3.34 mmol, 345 μL) of 3,3-dimethyloxetane. The mixture was then stirred for 14 h at room temperature. 3,3-Dimethyl-4-[(trimethylsilyl)oxy]butyronitrile was found in 86% yield. It had the following spectral properties: ^{1}H NMR δ 0.086 (s, 9 H), 0.999 (s, 6 H), 2.278 (s, 2 H), 3.291 (s, 2 H); ^{13}C (A) NMR δ 0.229, 24.342, 27.492, 35.686, 69.681, 117.938; MS, m/e 170 (M − 15, 100), 155 (23), 140 (25), 129 (51), 103 (34.6), 86 (22.9), 84 (35.7), 73 (64.9); IR 2250 (C≡N), 1250 (SiCH$_3$), 1080 cm^{-1} (SiO). Anal. Calcd for $C_9H_{19}NOSi$: C, 58.32; H, 10.33; N, 7.56. Found: C, 58.19; H, 10.24; N, 7.41.

Reaction of 2-Methyloxetane with Trimethylsilyl Cyanide. In a three-necked 10-mL round-bottomed flask equipped with a reflux condenser were placed 0.74 g (7.5 mmol, 1.0 mL) of trimethylsilyl cyanide and 0.2 mL of diethylaluminum chloride solution. To this was added 0.67 g (9.3 mmol, 0.8 mL) of 2-methyloxetane over a period of 1 h. The resulting mixture was allowed to react for 24 h at room temperature. GLC analysis of the resulting reaction mixture showed the formation of 4-methyl-4-[(trimethylsilyl)oxy]butyronitrile (47% yield). It had spectral properties in agreement with those reported by Matsuda.[8] MS, m/e 156 (M − 15, 56.9), 75 (100), 73 (53.9).

Reaction of Oxetane with Trimethylsilyl Cyanide. In a two-necked 2-mL round-bottom flask equipped with a reflux condenser were placed 0.221 g (2.23 mmol, 295 μL) of trimethylsilyl cyanide and 25 μL of diethylaluminum chloride solution. To this was added via syringe 0.184 g (3.17 mmol, 205 μl) of oxetane over a period of 1 h. The mixture was then allowed to react at room temperature for 18 h. 4-[(Trimethylsilyl)oxy]butyronitrile was obtained in 100% yield. It had spectral properties identical with an authentic sample prepared by the reaction of hexamethyldisilazane with γ-butyrolactone.[9] In the absence of diethylaluminum chloride no reaction occurred even after 72 h. 4-[(Trimethylsilyl)oxy]butyronitrile: ^{1}H NMR δ 0.13 (s, 9 H), 1.9 (m, 2 H), 2.45 (t, 2 H, J = 6.6 Hz), 3.69 (t, 2 H, J = 5.6 Hz); ^{13}C (A) NMR δ 0.162, 14.320, 28.747, 60.030, 117.6; IR 2250 (C≡N), 1250 (SiCH$_3$), 1080 cm^{-1} (SiO); MS, m/e 142 (M − 15, 100), 75 (57.9).

Reaction of Propylene Oxide with Trimethylsilyl Cyanide. In a three-necked 10-mL round-bottomed flask equipped with a reflux condenser was placed a mixture of 0.2 mL of diethylaluminum chloride solution and 0.97 g (9.8 mmol, 1.3 mL) of trimethylsilyl cyanide. To this was added 0.60 g (10 mmol, 0.7 mL) of propylene oxide over a period of 0.5 h. The mixture was then stirred at room temperature for 24 h. GLC analysis of the reaction mixture showed the formation of 3-methyl-3-[(tri-

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methylsilyl)oxy]propionitrile (83% yield). Its spectral properties were in complete agreement with those previously reported by West.[10] MS m/e 142 (M − 15, 62.1), 101 (96.8), 98 (100), 73 (89.7).

Reaction of Isobutylene Oxide with Trimethylsilyl Cyanide. In a two-necked 2-mL round-bottomed flask equipped with reflux condenser, was placed a mixture of 10 μL of diethylaluminum chloride solution and 0.116 g (1.17 mmol, 155 μL) of trimethylsilyl cyanide. To this was added 0.89 g (1.23 mmol) of isobutylene oxide over a period of 45 min. The mixture was then stirred for 48 h at room temperature. GLC analysis of this mixture revealed the formation of 3-methyl-3-[(trimethylsilyl)-oxy]butyronitrile (52% yield). A similar reaction with aluminum chloride as catalyst gave the same product (20%). 3-Methyl-3-[(trimethylsilyl)oxy]butylronitrile had the following spectral properties: ^{1}H NMR δ 0.193 (s, 9 H), 1.430 (s, 6 H), 2.482 (s, 2 H); ^{13}C (B) NMR δ 3.215 (q), 30.103 (q), 34.592 (t), 71.899 (s), 117.400 (s); IR 2251 (C≡N), 1260 (SiCH$_3$), 1050 cm^{-1} (SiO).[11]

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Registry No. Trimethylsilyl cyanide, 7677-24-9; 3,3-dimethyloxetane, 6921-35-3; 3,3-dimethyl-4-[(trimethylsilyl)oxy]butyronitrile, 81956-58-3; 2-methyloxetane, 2167-39-7; 4-methyl-4-[(trimethylsilyl)oxy]butyronitrile, 66408-81-9; oxetane, 503-30-0; 4-[(trimethylsilyl)oxy]butyronitrile, 72049-81-1; propylene oxide, 75-56-9; 3-methyl-3-[(trimethylsilyl)oxy]propionitrile, 31649-95-3; isobutylene oxide, 558-30-5; 3-methyl-3-[(trimethylsilyl)oxy]butyronitrile, 14904-41-7; 2,2-dimethyl-3-[(trimethylsilyl)oxy]propionitrile, 42202-45-9.

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Nitrogen-15 Nuclear Magnetic Resonance Studies of Benzenediazonium Ions. Effects of Solvent, Substituent, Anion, and 18-Crown-6[†1a]

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Effects of solvent change on the ^{15}N resonance positions for *p-n*-butylbenzenediazonium tetrafluoroborate are small. In contrast, the influence of substituents on the ^{15}N chemical shifts for para-substituted benzenediazonium tetrafluoroborates in acetonitrile are relatively large. For the *p-n*-butylbenzenediazonium cation in dichloromethane, replacement of the tetrafluoroborate anion by chloride produces small downfield shifts of the ^{15}N resonance positions for both nitrogens. Complexation of benzenediazonium tetrafluoroborates by 18-crown-6 in *N,N*-dimethylformamide induces relatively large changes in the ^{15}N chemical shifts. Attempts to detect crown ether complexation of other species with diazonium-like termini by ^{15}N NMR were unsuccessful.

A variety of spectroscopic methods[2] have been employed to assess the influence of aromatic ring substituents, solvents, anions, and specific complexing agents such as crown ethers[3] upon the structure and bonding of benzenediazonium ions. Infrared and ultraviolet spectral studies have recently been augmented by investigations which utilize ^{1}H and ^{13}C NMR.[4-7] Although it is a technique which could potentially provide much additional information, ^{15}N NMR spectroscopy has rarely been applied to the study of aromatic diazonium salts. Only ^{15}N chemical shifts of five benzenediazonium tetrafluoroborates solubilized[8] by 1.2–1.8 equiv of 18-crown-6 in CDCl$_3$ have been reported.[9]

Experimental difficulties encountered in making natural-abundance ^{15}N NMR measurements for uncomplexed benzenediazonium salts include problems of diazonium salt solubility in most organic solvents and of stability during the long pulse delays and numerous transients which are required. However, we have overcome these difficulties and report here the effects of solvent, substituent, and anion on the ^{15}N chemical shifts for N1 and N2 of uncomplexed benzenediazonium salts as well as the changes in these chemical shifts when 18-crown-6 is present.

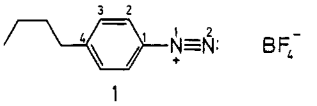
Results and Discussion

The solubility of benzenediazonium salts in organic solvents may be significantly enhanced by the attachment of lipophilic groups at the para position.[3,5,7] Natural-abundance ^{15}N NMR spectra of *p-n*-butylbenzenediazonium tetrafluoroborate (1) were measured in six organic

Table I. Effect of Solvent on the ^{15}N and ^{13}C NMR Chemical Shifts of 1[a]

solvent	chemical shift, δ				
	N1[b]	N2[b]	C1[c]	C4[c]	B[d]
dichloromethane	143.8	58.1	110.1	160.4	43
nitromethane	143.6	58.8	110.4	160.9	59
acetonitrile	143.5	58.8	111.2	160.6	103
acetone	144.0	59.7	111.9	159.8	123
1,4-dioxane	144.4	59.9	112.2	159.5	128
N,N-dimethylformamide	143.7	60.3	112.0	161.0	166

[a] Corrected for diamagnetic susceptibility of solvent.[10] (The largest correction, for nitromethane, was 1.4 ppm upfield.) [b] Upfield from external 1 M H^{15}NO$_3$ in D$_2$O. [c] Downfield from external Me$_4$Si. [d] Lewis basicity parameter.[11]



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[†] Contribution No. 6379 from the Gates and Crellin Laboratories.

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