

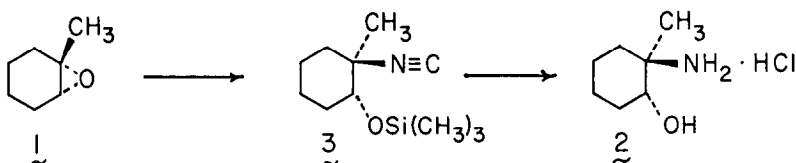
Regiospecific Opening of Oxetanes with Trimethylsilyl Cyanide - Zinc Iodide. A General Approach to γ -Amino Alcohols.

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Summary: Trimethylsilyl ethers of γ -hydroxy isonitriles were formed regiospecifically in the opening of oxetanes with trimethylsilyl cyanide - zinc iodide. Deprotection and hydrolysis of the initially formed ring cleavage products gave γ -amino alcohols.

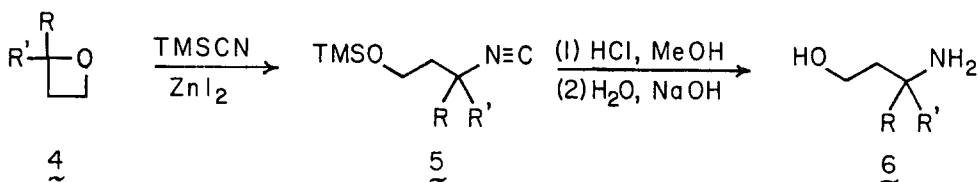
Recently, we described^{2,3} the opening of epoxides with trimethylsilyl cyanide and zinc iodide to yield trimethylsilyl ethers of β -hydroxy isonitriles. We also elucidated the regiochemistry and stereochemistry of these epoxide ring cleavages, and converted the initially formed products into β -amino alcohols. This is illustrated by the conversion of 1 into 2 via the



intermediacy of 3. Since epoxides and oxetanes are quite similar in strain energy,⁴ we explored the opening of these four-membered oxygen-containing heterocyclics with trimethylsilyl cyanide (TMSCN) and zinc iodide. We now wish to report the high-yield conversion of oxetanes into γ -amino alcohols via the intermediacy of γ -hydroxy isonitriles.

In a general procedure, one equivalent of a 0.6 M solution of the oxetane (4) in methylene chloride was added dropwise over 0.5 h to a refluxing solution containing two equivalents of trimethylsilyl cyanide (1.2 M in methylene chloride) and 5 mol percent of zinc iodide. After an

appropriate period of reflux, filtration through a plug of silica gel, and removal of the solvent, the product was purified by distillation. As shown in Table 1, the yields of the isonitriles, 5, ranged from 73 to 94%.¹⁰ The structures of the isonitriles were established on the



- $4a^5$ R = R' = H
 $4b^6$ R = CH₃, R' = H
 $4c^7$ R = R' = CH₃
 $4d^8$ R = C₆H₅, R' = H
 $4e^9$ R = CH=CH₂, R' = H

Table 1. Conversion of Oxetanes to Trimethylsilyl Ethers of γ -Hydroxy Isonitriles via Ring Cleavage with Trimethylsilyl Cyanide - Zinc Iodide.

Oxetane	Reflux Period	Isonitrile	% Yield ^a
4a	12 h	5a	94
4b	12 h	5b	76
4c	24 h	5c	77
4d	12 h	5d	91
4e	30 min	5e	73

(a) All yields are of purified (distilled) product.

basis of mass spectrometry, and infrared, ¹³C NMR and ¹H NMR spectroscopy. Particularly diagnostic was the occurrence of the isonitrile absorption in the infrared spectrum at 2120-2140 cm⁻¹. In addition, the appearance of nitrogen-14 coupling to each of the attached carbons provided conclusive evidence for the presence of the isonitrile moiety.^{2,11} Overall, this ring cleavage of oxetanes by trimethylsilyl cyanide - zinc iodide appeared to be quite general.¹²

Hydrolysis of 5 to the corresponding γ -amino alcohols was readily accomplished. In a general procedure, sufficient methanol to prepare a 0.75 M solution of 5 was placed in a flask at 0 °C and saturated with gaseous hydrogen chloride. The isonitrile, 5, was then added dropwise

Table 2. Yields of **6** Obtained from the Hydrolysis of the Isonitriles, **5**.

<u>Isonitrile</u>	<u>γ -Amino Alcohol</u>	<u>% Yield^a</u>
5a	6a ¹³	65
5b	6b ¹⁴	71
5c	6c ¹⁵	74
5d	6d ¹⁶	81

(a) All yields are of purified (distilled) product.

over a 15-min period, and the reaction mixture was allowed to warm to 24 °C and stirred at that temperature for 12 h. Isolation of the product and purification gave the yields listed in Table 2. All of the γ -amino alcohols prepared had been previously reported.¹³⁻¹⁶ However, since detailed characterization was lacking in the literature reports, **6a-d** were rigorously characterized by a combination of mass spectrometry and IR, ¹³C NMR, and ¹H NMR spectroscopy.

It should be recognized that the opening of the oxetanes by trimethylsilyl cyanide - zinc iodide was regiospecific. In all cases the isonitrile moiety was attached to the carbon center which should have been the most electropositive when the Lewis acid, zinc iodide, was complexed with the oxetane oxygen. Thus, our procedure leads to certain γ -amino alcohols which would be difficult to prepare by other methods.

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