CHEMISTRY LETTERS, pp. 481-484, 1990.

# Solid Base-directed Regioselective Ring Opening of Epoxides with Cyanotrimethylsilane

Keisuke SUGITA, Akihisa OHTA, Makoto ONAKA,* and Yusuke IZUMI*
Department of Synthetic Chemistry, Faculty of Engineering,
Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464

Calcium oxide and magnesium oxide are found to be effective solid bases for nucleophilic ring opening of epoxides with cyanotrimethylsilane to afford β-trimethylsiloxy nitriles in a highly regioselective manner without any contamination of isocyanides.

Cyanotrimethylsilane (TMSCN) has been reported to react with epoxides under catalysis of various Lewis acids to give β-trimethylsiloxy nitriles or β-trimetylsiloxy isocyanides; "hard" acids such as $AlCl_3$,$^{1,2)}$ $Et_2AlCl$,$^{1,3)}$ $Al(O^iPr)_3$,$^{3)}$ $LnCl_3$,$^{4)}$ and $Ti(O^iPr)_4$$^{5)}$ promoted the reaction to afford nitriles, while isocyanides were produced by the action of "soft" acids such as $ZnI_2$,$^{6)}$ $Pd(CN)_2$,$^{3)}$ and $SnCl_2$.$^{3)}$ However in **acid**-promoted nitrile formation the problems are often encountered of low regioselectivity in ring openings of unsymmetrical epoxides and contamination of isocyanides. Here we wish to describe the first example of **base**-catalyzed ring openings of epoxides with TMSCN to produce exclusively β-trimethylsiloxy nitriles in a highly regioselective manner.

Recently we discovered that basic inorganic salts could activate TMSCN to react with various carbonyl compounds to afford trimethylsilylated cyanohydrins.$^{7)}$ Thus we searched inorganic solid bases suitable for ring opening of epoxides with TMSCN. Table 1 summarizes the results of the reaction of 1,2-epoxyoctane with TMSCN in the presence of solid catalyst in heptane.$^{8)}$ On solid bases such as CaO, MgO, hydroxyapatite (HAp, $Ca_{10}(PO_4)_6(OH)_2$),$^{9)}$ and $CaF_2$,$^{9)}$ the ring opening of the epoxide was accelerated to produce 3-(trimethylsiloxy)nonanenitrile ($\underline{1}$) in over 97% regioselectivity. The catalytic activity of solid base decreased in the order of CaO $\fallingdotseq$ MgO > HAp >> $CaF_2$, correlating to the intrinsic base strength of the solid. In contrast to the solid bases, strongly acidic montmorillonite (Fe-Mont) as well as weakly acidic silica ($SiO_2$) showed no

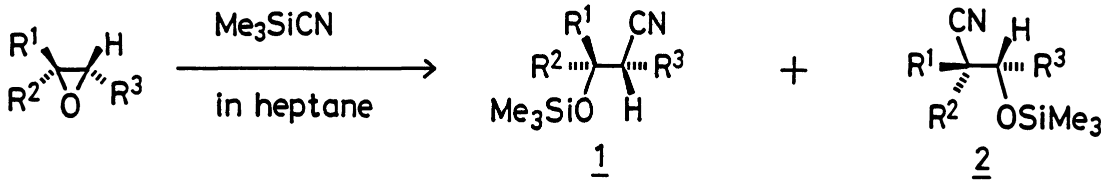

Table 1. Ring opening of 1,2-epoxyoctane ($R^1=C_6H_{13}$, $R^2=R^3=H$) with TMSCN[a]

| Run | Solid catalyst | S.A.[b] /$m^2g^{-1}$ | Acid or base strength[c] | Time /h | Yield /% | 1 : 2 |
|---|---|---|---|---|---|---|
| 1 | CaO | 65 | $H_- \geq +18.4$ | 0.5 | 97 | 97 : 3 |
| 2 | MgO | 316 | $H_- \geq +18.4$ | 0.5 | 98 | 98 : 2 |
| 3 | HAp[d] | 55 | $+15.0 > H_- \geq +9.3$ | 1.5 | 97 | 98 : 2 |
| 4 | $CaF_2$ | 6 | e) | 72 | 96 | 99 : 1 |
| 5 | $SiO_2$ | 585 | $+3.3 \geq H_0 > +1.5$ | 5 | 0 | |
| 6 | Fe-Mont[f] | 37 | $-8.2 \geq H_0$ | 5 | 0 | |

a) Catalyst (0.2 g), 1,2-epoxyoctane (1 mmol), TMSCN (2 mmol), in heptane, at room temperature. b) Specific surface area.
c) Maximum acid or base strength determined with Hammett indicators.
d) Hydroxyapatite. e) $H_-$ of $CaF_2$ could not be determined.
f) Ferric ion-exchanged montmorillonite.

Table 2. CaO-directed ring opening of unsymmetrical epoxides with TMSCN[a]

| Run | $R^1$ | $R^2$ | $R^3$ | Time/h | Yield/% | 1 : 2 |
|---|---|---|---|---|---|---|
| 7 | $CH_3$ | $CH_3$ | H | 0.5 | 98 | > 99 : 1 |
| 8 | $CH_3$ | $-(CH_2)_4-$ | | 4.5 | 95 | 99 : 1 |
| 9 | $CH_3$ | $CH_3$ | $CH_3$ | 24 | 84 | 94 : 6 |

a) CaO (0.2 g), epoxides (1 mmol), and TMSCN (2 mmol), in heptane, at room temperature.

catalytic activity for the ring opening. We presume that strongly basic sites of $O^{2-}$ on the surface of CaO and MgO[10] coordinate to TMSCN to release a cyanide ion, resulting in nucleophilic ring opening of epoxides.

Table 2 shows ring openings of unsymmetrical epoxides with TMSCN on CaO. All the epoxides we investigated quantitatively afforded β-trimethylsiloxy nitriles by highly regioselective (>94%) attack of cyanide on the less substituted carbon of epoxides without any formation of isocyanides (Runs 7-9). The ring opening in Run 8 completely occurred in an $S_N2$

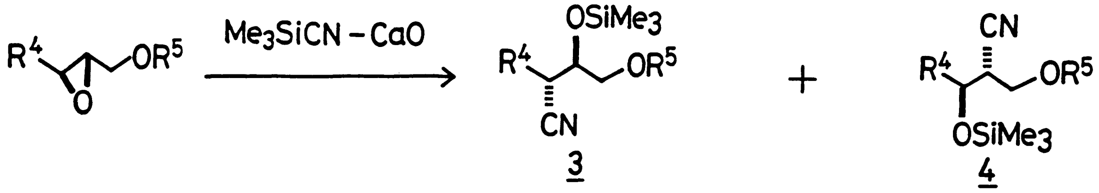

Table 3. CaO-directed reactions of 2,3-epoxy 1-ol and its derivative with TMSCN[a)]

| Run | $R^4$ | $R^5$ | Conditions[a)] Temp/$^o$C, (Time/h) | Yield/% | 3 : 4 |
|---|---|---|---|---|---|
| 10 | $^n$Pr | H | r.t. (4) | 86 | 89 : 11 |
| 11 | $^n$Pr | Ac | r.t. (4) | 91 | 96 : 4 |
| 12 | $^i$Pr | Ac | 60$^o$C (1) | 75 | 96 : 4 |
| 13 | Cyclohexyl | Ac | 60$^o$C (2) | 84 | 97 : 3 |

a) CaO (0.5 g), epoxides (0.5 mmol), TMSCN (1 mmol), in heptane.

fashion.

Regioselective ring openings of 2,3-epoxy 1-ols with nucleophiles are intriguing studies since easily available, optically pure 2,3-epoxy 1-ols are important building blocks for synthesis of natural products. On CaO, ring opening of 2,3-epoxyhexan-1-ol with TMSCN smoothly took place to afford products of 3 and 4 in good yield (86%) and good regioselectivity (89:11). We assume that the high regioselection is attributed to formation of a five-membered chelate complex between two oxygen atoms of the epoxyalcohol and a calcium ion in CaO, which directs a ring-opening site.[11)] In the present reaction the epoxyalcohol was found to be initially converted with TMSCN to 1-trimethylsiloxy epoxide, and then underwent nucleophilic ring opening. The bulky trimethylsilyl group would prevent the chelate formation. In order to improve regioselectivity in the ring opening, 2,3-epoxy 1-ol was acetylated and then treated with TMSCN on CaO. Highly regioselective ring openings at the C-3 carbon were realized as shown in Table 3. In Runs 10-13 the ring openings proceeded with inversion of configuration, and no isocyanides were formed. MgO, HAp, and $CaF_2$ showed lower activity than CaO. $Ti(O^iPr)_4$ was reported to promote the reaction of 2,3-epoxyhexan-1-ol with TMSCN under DME reflux conditions to give C-3 and C-2 opening products in 83:17 regioselectivity and 32% yield.[5a)] Compared with the Lewis acid-promoted reaction, CaO-catalyzed ring openings proceed more efficiently and regioselectively because CaO serves as a bifunctional catalyst; an oxide anion on CaO activates TMSCN and simultaneously a calcium ion on CaO activates an epoxyalcohol as a Lewis acid and regulates the ring opening.

As solid catalysts are easily separable from organic products through simple filtration, pure cyanosilylated products are obtainable without hydrolysis.

A typical experimental procedure is as follows: In a flask a solid catalyst (0.2 g) was dried at 0.5 Torr for 3 h (drying temperature: HAp, 500 °C; $CaF_2$, 180 °C; $SiO_2$, 200 °C; Fe-Mont, 120 °C). CaO and MgO were prepared from $Ca(OH)_2$ and $Mg(OH)_2$ by calcination at 500 °C and 0.5 Torr for 2 h. To a suspended mixture of the solid catalyst and heptane (2 ml) were added a heptane solution (3 ml) of epoxide (1 mmol), and TMSCN (2 mmol), successively. The mixture was stirred under the conditions shown in Tables. After consumption of the epoxide, the solid catalyst was filtered off through a Celite pad. The filtrate was distilled to yield products. The regioisomeric ratios of the products were determined by $^1H$ NMR (200 MHz) or capillary GLC (OV-1, 25m).

References

1) J. C. Mullis and W. P. Weber, J. Org. Chem., 47, 2873 (1982).

2) W. Lidy and W. Sundermeyer, Tetrahedron Lett., 1973, 1449.

3) K. Imi, N. Yanagihara, and K. Utimoto, J. Org. Chem., 52, 1013 (1987).

4) A. E. Vougioukas and H. B. Kagan, Tetrahedron Lett., 28, 5513 (1987).

5) a) M. Caron and K. B. Sharpless, J. Org. Chem., 50, 1557 (1985);
b) M. Emziane, P. Lhoste, and D. Sinou, J. Mol. Catal., 49, L23 (1988).

6) P. G. Gassman and T. L. Guggenheim, J. Am. Chem. Soc., 104, 5849 (1982); P. G. Gassman and R. S. Gremban, Tetrahedron Lett., 25, 3259 (1984); P. G. Gassman and L. M. Haberman, ibid., 26, 4971 (1985); P. G. Gassman, K. Okuma, A. Lindbeck, and R. Allen, ibid., 27, 6307 (1986); P. G. Gassman and L. M. Haberman, J. Org. Chem., 51, 5010 (1986).

7) M. Onaka, K. Higuchi, K. Sugita, and Y. Izumi, Chem. Lett., 1989, 1393.

8) A less polar solvent is preferable in order to increase the reaction rate; the reaction of 1,2-epoxyoctane with TMSCN was performed at r.t. in various solvents by use of MgO (reaction time, yield, ratio of 1:2): heptane (0.5 h, 98%, 98:2); benzene (0.5 h, 97%, 98:2); dichloromethane (0.5 h, 97%, 99:1); 1,2-dimethoxyethane (3 h, 95%, 96:4).

9) HAp and $CaF_2$ can activate TMSCN as anionic catalysts: see Ref. 7.

10) The basic site on CaO or MgO was reported to be a surface lattice oxygen ($O^{2-}$): K. Tanabe and K. Saito, J. Catal., 35, 247 (1974).

11) M. Onaka, K. Sugita, and Y. Izumi, J. Org. Chem., 54, 1116 (1989).

(Received January 5, 1990)