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MECHANISTIC INSIGHTS INTO THE OPENING OF EPOXIDES WITH TRIMETHYLSILYL CYANIDE - ZINC IODIDE

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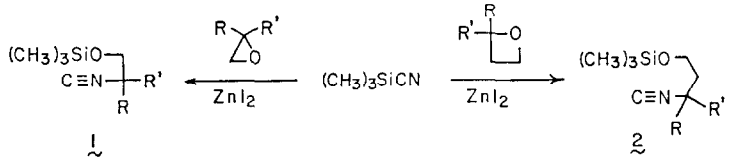
Summary: endo-2,3-Epoxy-1,7,7-trimethylbicyclo[2.2.1]heptane reacted with trimethylsilyl cyanide in the presence of zinc iodide to produce a complex mixture of products. The major product, anti-7-trimethylsiloxy-endo-2,3,3-trimethyl-exo-2-isocyanobicyclo[2.2.1]heptane was obtained in 72% yield. In addition, eight other products were identified in yields ranging from 10% to 1%. All of the products could be rationalized on the basis of initial generation of a carbocationic intermediate.

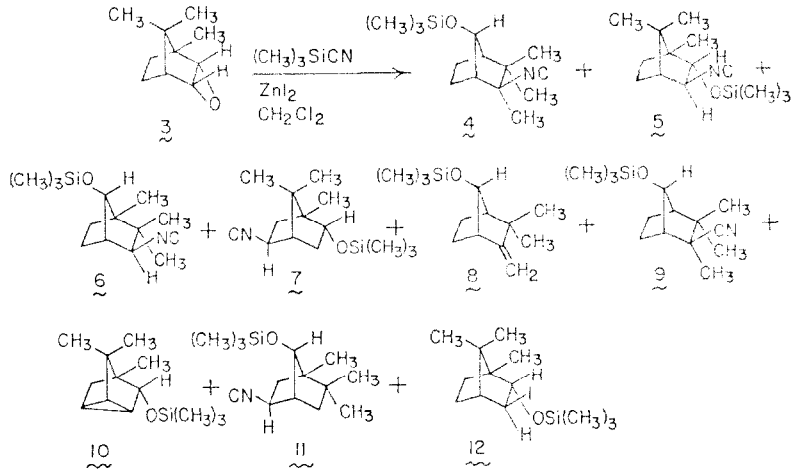
Recently, we have described the opening of oxiranes (epoxides)[3] and oxetanes[4] with trimethylsilyl cyanide - zinc iodide to produce high yields of **1** and **2**, respectively. Because of the ease with which **1** could be converted into β-amino alcohols and **2** into γ-amino alcohols,



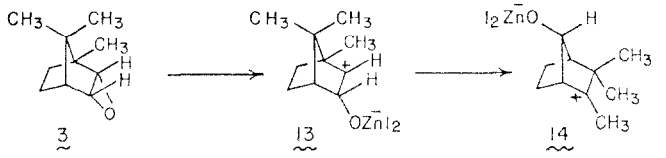
these reactions appear to have considerable synthetic potential. In view of this synthetic utility, an in-depth understanding of the mechanistic aspects of these ring opening reactions was desirable. This paper provides a detailed study of the opening of racemic endo-2,3-epoxy-1,7,7-trimethylbicyclo[2.2.1]heptane (**3**)[5] with trimethylsilyl cyanide (TMSCN) - zinc iodide, which indicates the intermediacy of several different carbocationic species.

When **3** was treated with TMSCN and ZnI_2 (1 mol %) at 25 °C for three days, we obtained a complex mixture of products in 97% total yield. All products were purified and their structures were determined by a combination of infrared spectroscopy, ^1H NMR, ^{13}C NMR, 2D-NMR, mass spec-

trometry and, for **4** and **9**, by single crystal X-ray structure determination.[6-9] The yields of the various components were: **4**, 72%; **5**, 10%; **6**, 3%; **7**, 3%; **8**, 3%; **9**, 2%, **10**, 2%, **11**, 1%; **12**, 1%.[10]



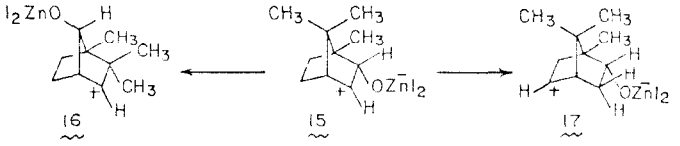
The structure of **4**, mp 63.5-64.2 °C, was unequivocally established on the basis of single crystal X-ray analysis. Clearly, this major product resulted from a classical cationic rearrangement of the bicyclo[2.2.1]heptyl skeleton. This rearrangement would appear to involve the



initial formation of **13** followed by rearrangement to **14**. Collapse of the tertiary cation **14** with TMSCN would then yield **4**.

Compound **5** is the straightforward product from ring opening without rearrangement. If the reaction involved only an S_N2 attack by TMSCN on the ZnI_2 complexed epoxide, **5** would be the only expected product. Whether **5** resulted from collapse of **15** with TMSCN or via direct S_N2 attack on the Lewis acid complex, **3**, cannot be determined from the available data.

Compounds **6** and **7** would appear to be derived from more complex processes. However, each

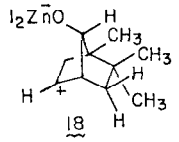


requires a rearrangement, which is best rationalized in terms of a series of carbocationic

intermediates. In order to obtain **6**, **3** would have to open to produce **15** which on rearrangment would give **16**. Collapse of **16** with TMSCN would give **6**. For the production of **7**, the ion **15** would also be involved. In this case a [5,3]-hydride shift would give **17**, which on reaction with TMSCN would yield **7**.

Compound **8** can be viewed as the product derived from proton loss from **14**. Compound **9** is also derived from **14**, but represents a highly unusual example where **14** captures the cyanide rather than the isonitrile moiety. Had this compound not been crystalline and susceptible to single crystal X-ray determination, its structure proof would have been exceedingly difficult.

The formation of **10** offers excellent evidence for the discrete existence of **15**. Loss of a proton from the 5-position of **15** would produce **10**. The formation of **11** is best rationalized



18

through the intermediacy of **16**. A [5,3]-hydride shift in **16** would produce **18**. TMSCN would be expected to react with **18** to produce **11**. Lastly, **12** would result from addition of the trimethylsilyl group and of iodide to **15**.

All of the products derived from the reaction of **3** with TMSCN-ZnI_2 can be rationalized in terms of the intermediacy of carbocationic intermediates. Clearly, the formation of **4**, **6**, **7**, **8**, **9**, **10**, and **11** can only be explained via carbocationic rearrangement. The stereochemistry of the isonitrile and iodide moieties of the minor products, **5** and **12**, respectively, could be explained on the basis of either a carbocationic intermediate, or S_N2 attack on the Lewis acid complexed epoxide.

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References and Footnotes

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4. Gassman, P. G.; Haberman, L. M. Tetrahedron Lett. **1985**, 26, 4971. See also: Carr, S. A.; Weber, W. P. Synth. Commun. **1985**, 15, 775.
5. Suzuki, A.; Miki, M.; Itoh, M. Tetrahedron **1967**, 23, 3621. We obtained **3** with a mp 169.0-170.5 °C (lit.[5] mp 171-172 °C).
6. Satisfactory elemental analyses and/or exact mass molecular weights were obtained for all new compounds.
7. Spectral data and physical constants for compounds **4-12** are: **4:** mp 63.5-64.2 °C; IR (KBr) 2120 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.56 (1 H), 2.08 (1 H), 1.62-1.78 (3 H), 1.42-1.55 (1 H), 1.34-1.39 (1 H), 1.32 (3 H), 1.18 (3 H), 0.90 (3 H), 0.12 (9 H); ^{13}C NMR ($CDCl_3$) δ 0.12, 19.51, 20.53, 21.25, 22.45, 28.60, 39.72, 53.38, 56.04, 66.51 (t), 75.69, 154.09 (t). **5:** IR (neat) 2132 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.09 (1 H), 2.90 (1 H), 1.87 (1 H), 1.59 (1 H), 1.35 (1 H), 1.02 (3 H), 0.87 (1 H), 0.75 (1 H), 0.68 (3 H), 0.57 (3 H), 0.05 (9 H); ^{13}C NMR ($CDCl_3$) δ -0.02, 12.72, 19.06, 20.66, 24.72, 26.61, 47.41, 50.34, 51.62, 64.35 (t), 84.06, 156.76 (t). **6:** IR (neat) 2135 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.00 (1 H), 2.58 (1 H), 1.96 (1 H), 1.73 (1 H), 1.48 (1 H), 1.15 (1 H), 0.94 (3 H), 0.73 (3 H), 0.67 (1 H), 0.52 (3 H), 0.15 (9 H); ^{13}C NMR ($CDCl_3$) δ 0.13, 12.80, 24.22, 24.93, 24.99, 28.33, 39.91, 50.13, 51.02, 64.32 (t), 78.70, 155.97 (t). **7:** IR (neat) 2143 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.80 (1 H), 3.56 (1 H), 2.57 (1 H), 2.22 (1 H), 2.02 (1 H), 1.61 (1 H), 1.15 (3 H), 0.88 (3 H), 0.83 (3 H), 0.78 (1 H), 0.06 (9 H); ^{13}C NMR ($CDCl_3$) δ 0.11, 12.58, 19.43, 21.04, 36.32, 38.14, 48.16, 50.72, 51.95, 54.16 (t), 75.03, 154.21 (t). **8** (The trimethylsilyl ethers, **8** and **10**, could not be preparatively separated. Thus, these compounds were cleaved to the corresponding alcohols, which were readily separated, and the alcohols were characterized. Data reported for **8** and **10** are for the corresponding alcohols): mp 92-94 °C; IR (KBr) 3440, 1782 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.68 (1 H), 4.50 (1 H), 4.23 (1 H), 2.46 (1 H), 1.90 (1 H), 1.75-1.62 (3 H), 1.48 (1 H), 1.25 (1 H), 0.99 (3 H), 0.98 (3 H); ^{13}C NMR ($CDCl_3$) δ 20.50, 25.74, 26.16, 29.39, 41.01, 51.47, 52.17, 77.50, 101.56, 162.98. **9:** mp 79-80 °C; IR (KBr) 2230 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.53 (1 H), 2.15 (1 H), 1.68-1.73 (2 H), 1.64 (1 H), 1.45-1.59 (2 H), 1.27 (6 H), 0.91 (3 H), 0.14 (9 H); ^{13}C NMR ($CDCl_3$) δ 0.16, 17.78, 18.65, 20.39, 22.06, 30.40, 38.18, 42.42, 53.37, 53.65, 76.44, 124.88. **10** (characterized as corresponding alcohol):[8] mp 130-131 °C; IR (KBr) 3380 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.73 (1 H), 1.46 (1 H), 1.38 (1 H), 1.29 (1 H), 1.20-1.10 (3 H), 0.77 (3 H), 0.75 (3 H), 0.74 (3 H); ^{13}C NMR ($CDCl_3$) δ 8.01, 13.61, 19.53, 20.01, 21.81, 27.23, 33.34, 43.03, 45.58, 79.45. **11:** IR (neat) 2145 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.83 (1 H), 3.44 (1 H), 2.21 (1 H), 2.12 (1 H), 1.94 (1 H), 1.41 (1 H), 0.95 (1 H), 0.88 (3 H), 0.87 (3 H), 0.82 (3 H), 0.08 (9 H); ^{13}C NMR ($CDCl_3$) δ 0.05, 11.84, 25.29, 28.77, 34.88, 39.12, 40.68, 49.13, 51.77, 54.38 (t), 80.02, 153.20 (t). **12:** IR-no nitrile, isonitrile, or unsaturation; ^1H NMR ($CDCl_3$) δ 4.33 (1 H), 3.61 (1 H), 2.07 (1 H), 1.94 (1 H), 1.71 (1 H), 1.29 (1 H), 1.28 (3 H), 1.12 (1 H), 0.81 (3 H), 0.79 (3 H), 0.17 (9 H); ^{13}C NMR ($CDCl_3$) δ 0.76, 13.41, 20.37, 21.32, 24.90, 30.44, 36.18, 47.68, 52.15, 54.87, 88.26.
8. The alcohol derived from **10** provided spectral data identical to those of an authentic sample: Crandall, J. K.; Crawley, L. C.; Banks, D. B.; Liu, L. C. J. Org. Chem. **1971**, 36, 510. We wish to thank Professor Crandall for providing a sample of the optically active alcohol corresponding to that derived from desilylation of **10**.
9. X-ray data on compounds **4** and **9** will be provided in a separate paper on this subject.
10. Products are ordered in terms of decreasing yields. All yields have been rounded to the nearest percentage. At least four other extremely trace (<0.5%) components were detected by GLC analysis. The GLC order of elution of the identified components was **10, 8, 6, 5, 4, 11, 9, 7, 12** on an OV-101 capillary column.

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