Trimethylsilyl cyanide \([\text{CH}_3)_3\text{Si-CN}\] is a source of nucleophilic cyanide ion that, unlike sodium cyanide (NaCN), can dissolve readily in organic solvents. There are five different substitution and elimination products observed in the following reaction with compound W. What are they?

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{H}_3\text{C} \\
\text{H} & \quad \text{O} \\
& \quad \text{CF}_3 \\
& \quad (\text{H}_3\text{C})_3\text{Si-CN} \\
\text{DMF, heat} & \quad \text{substitution product C1} \\
& \quad \text{substitution product C2} \\
& \quad \text{elimination product C3} \\
& \quad \text{elimination product C4} \\
& \quad \text{elimination product C5}
\end{align*}
\]

When compound W reacts with potassium tert-butoxide \([\text{CH}_3)_3\text{COK}\], only three of these five products are observed. Of those three products, they can be ranked from major to minor based solely on the steric accessibility of the \(\beta\)-H that is being removed (more accessible = faster reaction). Using the C1 through C5 labels above, according to the products as you have entered them, rank the three anticipated outcomes from the reaction of compound W with potassium tert-butoxide as major to minor.

The following reaction produces two pairs of isomeric products derived from substitution and elimination pathways. Draw these pairs and indicate the stereochemical or structural relationship between them.
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If you are told that a reaction is one where substitution and elimination are happening, then possible outcomes can be anticipated:

There is one \(s^3\)C-LG and five \(\beta\)-Hs in two groups, 3 on one of the \(\beta\)-Cs and 2 on the other \(\beta\)-C.

Stereochemical analysis of these connectivities is exactly the same as any prior question, except that now it is assumed that you have this analysis method mastered and in place as a skill.

Every earlier topic will eventually show up in understanding reaction chemistry (which is why they are there in the first place… to build the foundation of ideas): relative acid-base strength and decisions based on \(pK_a\) values, relative rates and stabilities and whether the reaction is irreversible (kinetic control) or reversible (thermodynamic control), molecular structure and bonding features such as delocalization, hybridization, geometry, stereochemical analysis, and conformational analysis.

In this example, then, without regard to mechanism, it is possible to use the definition of “substitution” and “elimination” and stereochemical analysis to anticipate all of the POSSIBLE reaction products. This is the maximum number. Mechanistic understanding provides a way to narrow the prediction, sometimes to a single outcome from among all of these possibilities.
Trimethylsilyl cyanide [(CH$_3$)$_3$Si-CN] is a source of nucleophilic cyanide ion that, unlike sodium cyanide (NaCN), can dissolve readily in organic solvents. There are five different substitution and elimination products observed in the following reaction with compound W. What are they?

Before you even look at the problem, the text of the problem allows you to anticipate:
(a) substitution and elimination reaction outcomes are observed (so you need to have understood what those mean, as on the previous pages)
(b) there are five outcomes, so stereochemical analysis is likely
(c) the Lewis base (nucleophile) is the cyanide ion, which if you do not understand how to interpret the trimethylsilyl cyanide, the analogy of sodium cyanide is provided (so cyanide is CN$^-$)
(d) if cyanide is the nucleophile, and this is a substitution and elimination reaction, then compound W is anticipated to have an sp$^3$ C-LG bond in it

And, the analysis of the reactants:

- Possible sp$^3$ C-LG bond
- LB source : C≡N : 3 $\beta$-Hs, no source of stereoisomers for elimination reaction; 1 unique product
- DMF, heat conditions
- Possible sp$^3$ C-LG bonds, but no $\beta$-Hs for elimination!
- Not involved & so just re-copied in all
- Substitution here at a stereocenter means S$_N$ with retention and inversion are both possible

Before you write ANYTHING, a visual analysis of the problem identifies exactly what is explicitly asked for in the problem: 5 different substitution and elimination products: and the answer spaces affirm that there are 2 substitution products and 3 elimination products.

**Substitution product C1**
Retention of configuration

**Substitution product C2**
Inversion of configuration

**Elimination product C3**
Proper sp$^2$ geometry!

**Elimination product C4**
Proper sp$^2$ geometry!

**Elimination product C5**
Proper sp$^2$ geometry!
The following reaction produces two pairs of isomeric products derived from substitution and elimination pathways. Draw these pairs and indicate the stereochemical or structural relationship between them.

Although the text of this question is phrased in an open-ended way, at this point you still have a quite-limited number of possible chemical reactions to consider:

I. Lewis Acid-Base complexation/decomplexation

II. Bronsted Acid-Base proton transfer reactions

III. Substitution and Elimination reactions at sp³ C-LG bonds

The text also says that pairs of isomeric products are formed (two and two only, and they are either stereoisomers or structural isomers).

In this example, it states that two pairs are formed. Stepping through the possible reactions:

I. Lewis Acid-Base complexation/decomplexation - not possible as there are no open shell Lewis acids present

II. Bronsted Acid-Base proton transfer reactions - in principle, there are two protonations, but there are not four

III. Substitution and Elimination reactions at sp³ C-LG bonds - there is one sp³ C-electronegative atom bond which is a stereocenter, and it has 5 β-Hs in two groups (from the group of 3, no E/Z diastereomers; from the group of 2, you cannot produce both of the E/Z diastereomers because of the small ring constraint), so there are the two pairs

HCl + H₂O gives H₃O⁺ Cl⁻ a source of chloride ion as LB

substitution here at a stereocenter means S_N with retention and inversion are both possible

2 β-Hs here, but only 1 stereoisomer possible because of small ring constraint

3 β-Hs here, no source of stereoisomers for elimination reaction; 1 unique product

0 β-Hs here, no elimination reaction possible

Retention of configuration

 inversion of configuration

They are: enantiomers

They are: structural isomers