



PROBLEM 14

[SUPPL Problem 14 # 2]

More about stereoheterotopism, and *Re* vs *Si* nomenclature:

You are no doubt aware that Robert Cahn, Christopher Ingold and Vladimir Prelog [1] proposed a short series of unambiguous descriptors of asymmetric organic compounds: E/Z to replace *trans* and *cis* C=C, and the *R* and *S* designations to replace the L and D used earlier on the basis of $[\alpha]_D$ index, for chiral carbons and atoms with six substituents as well (S, P). Thus, the CIP system became accepted IUPAC rules.

A pending question remained, whose answer is less well known among students:

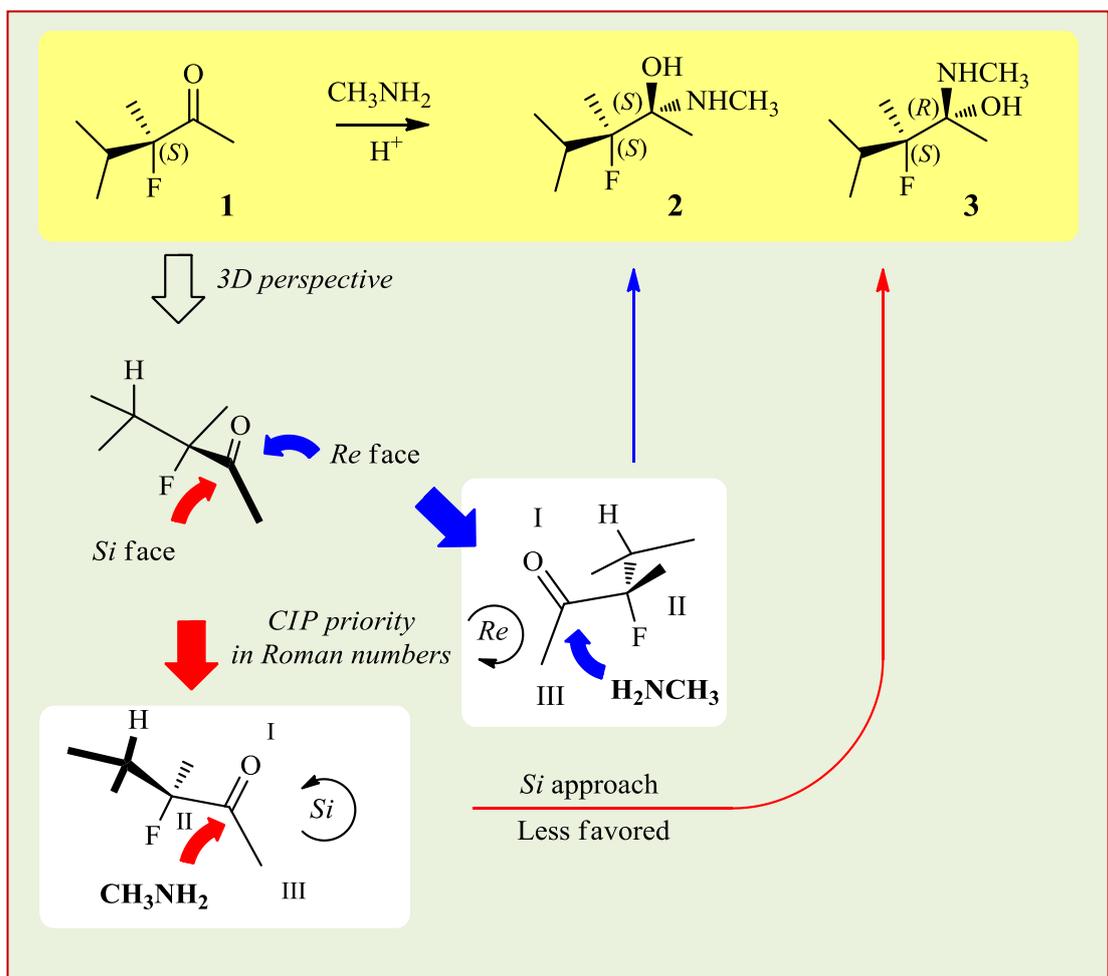
Imagine a trigonal reactive center such as C=O in a given compound whose substituents create different affinities with an incoming reagent, as a result of a chiral center in the vicinity. This affinity stems from attractive forces such as dipolar interaction and hydrogen bonding. As opposed to this, repulsive forces result usually in simple steric compression. In this circumstance the sides or *faces* of the C=O group are different. CIV refers to these faces as *enantiotopic* when the incoming nucleophile is achiral. The result will be a racemic product but one of the two may be favored.

Additionally, if the incoming nucleophile is chiral, then the faces of C=O are *diastereotopic*. Diastereoisomers result, likely in different proportion [2].

The term *stereoheterotopic face* is used to encompass either enantiotopic or diastereotopic trigonal centers [3].

The stereoheterotopic face of a *trigonal* atom is designated **Re** if the substituents (including the incoming compound) are arranged in the clockwise direction using the Cram-Ingold-Prelog (CIP) priority when viewed from that side of the face. The opposite is designated **Si**.

This concept is illustrated in the reaction of Scheme SP14.2.1. When asked to decide which product, **2** or **3**, is expected to prevail, the analysis should consider the *Si* and *Re* faces of ketone **1** because of reactivity asymmetries created by the vicinal chiral center. According to this analysis, the *Re* face of **1** is more exposed to methylamine and the expected mayor product should be the *S,S*-diastereomer **2**.



SCHEME SP14.2.1

The absolute configuration of the new chiral center that results is not necessarily associated: $Re \rightarrow (R)$ or $Si \rightarrow (S)$, but will depend on substrate and incoming reagent CIP priorities of the end product. The reaction of Scheme SP14.2.1 is precisely one such case.

REFERENCES

- [1] Cahn RS, Ingold CK, Prelog V. *Angew. Chem. Int. Ed.* 1966;5:385-415.
- [2] Moss GP. *Basic Terminology of Stereochemistry, IUPAC recommendations 1996.* *Pure & Appl. Chem.* 1996;68:2193-2222. Can be downloaded legally from:
<http://www.iupac.org/publications/pac/1996/pdf/6812x2193.pdf>
- [2] Hirschmann, *Trans NY Acad Sci* 1983, 41(1, ser II), 61-69.