Synthesis of trifluoromethylmethionine: Making sulfur chemically behave like selenium.

Sulfur and selenium are elements found in biology as constituent parts of nucleic acids and proteins, with sulfur being much more frequently used. We seek to address the fundamental chemical differences between sulfur and selenium that could explain why selenium replaces sulfur in some rare instances in biological macromolecules. Our hypothesis is that selenium is a Janus-faced element with respect to high nucleophilic and electrophilic character. An example of this is the oxidation of selenomethionine to methionine selenoxide, illustrating selenium's high nucleophilicity towards oxygen. This oxidation is reversible since methionine selenoxide can be reduced back to methionine with the addition of reducing agents. This illustrates the "electrophilic face" of selenium. In contrast, while methionine can be oxidized to methionine sulfoxide, this sulfoxide cannot be reduced back to methionine. This is because sulfur is worse at accepting electrons compared to selenium and is thus missing this "electrophilic face". The goal of this project is to create a sulfur-containing molecule that can chemically behave like selenium with respect to oxidation and reduction. This will be achieved by synthesizing trifluoromethylmethionine. The electron withdrawing α-fluorine atoms will make the adjacent sulfur atom of trifluoromethionne electron deficient. We predict that the sulfur atom of trifluoromethionine will be less nucleophilic than the sulfur atom of methionine, but it will be much more electrophilic. This will be determined by measuring the rates of oxidation and reduction of methionine, trifluoromethionine, and selenomethionine. We hope to illustrate fundamental chemical differences between sulfur and selenium in this study. One notable application of this molecule is that it should be able to act as a "redox switch" in designed peptides. This switch can be "turned on" by reduction and "turned off" by oxidation.