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A Potential Intermediate for the Aza-Corey–Chaykovsky Reaction: Synthesis, Structure, and Thermolysis of a Pentacoordinate 1,2-Thiazetidine 1-Oxide

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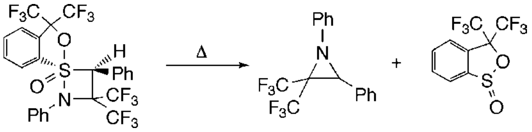
ABSTRACT



Thermolysis of a pentacoordinate $1\lambda^6$,2-thiazetidine, which was synthesized for the first time and characterized by X-ray crystallographic analysis, gave the corresponding aziridine and a cyclic sulfinate almost quantitatively. The potential intermediacy of a $1\lambda^6$,2-thiazetidine was suggested in the aza-Corey–Chaykovsky reaction.

The Corey−Chaykovsky reaction, the oxirane formation reaction from a sulfonium or oxosulfonium ylide and a carbonyl compound, is one of the most useful methods for preparation of oxiranes.[1] Its nitrogen version, the aza-Corey−Chaykovsky reaction, has been used for the synthesis of aziridines from a sulfonium[2] or oxosulfonium ylide[3] and an imine. Since the appearance this decade of highly stereoselective[4] and enantioselective[5] aza-Corey−Chaykovsky reactions, studies on the reaction mechanism are important to improve the selectivities. Some reaction mechanisms for the aza-Corey−Chaykovsky reaction of an oxosulfonium ylide have been postulated to date. One mechanism is the intramolecular attack of the imido anion on the β-carbon in the betaine (syn or anti), which is formed by the nucleophilic

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attack of the ylidic carbon on the imine carbon atom, with elimination of a sulfoxide[3b,c] or decomposition from a metal-containing six-membered ring transition state.[3d,e,g] Another proposed mechanism is the degradation of a pentacoordinate 1,2-thiazetidine, the [2 + 2]-cycloadducts of an oxosulfonium ylide and an imine.[3e] However, the intermediate of the aza-Corey−Chaykovsky reaction has neither been observed nor isolated, and the reaction mechanism has not yet been elucidated.

As a continuation of our work on the four-membered ring compounds bearing a highly coordinate chalcogen atom,[6] we previously demonstrated the oxirane formation reactions of tetracoordinate 1,2-oxathietanes **1**[6b] and pentacoordinate 1,2-oxathietanes **2**[6c,d] bearing the Martin ligand,[7] which are the [2 + 2]-cycloadducts of a sulfonium ylide and an oxosulfonium ylide with a carbonyl compound, respectively (Figure 1). Because some reports have advocated the contribution of a tetracoordinate 1,2-thiazetidine[6,8] and a pentacoordinate 1,2-thiazetidine[3e] as an intermediate in the aza-Corey−Chaykovsky reaction, it is important to elucidate the reactivity of the highly coordinate 1,2-thiazetidines for the study of the reaction mechanism of the aza-Corey−Chaykovsky reaction. However, no compound with such a ring system containing a pentacoordinate sulfur atom has been reported in contrast to a great number of reports on β-sultams and a few reports on dicoordinate 1,2-thiazetidine and tricoordinate 1,2-thiazetidine 1-oxides.[9] We report here the synthesis, crystal structure, and thermolysis of the first example of a pentacoordinate $1\lambda^6$,2-thiazetidine, a novel type of sulfurane oxide.[6c,10] We also discuss its comparison with a tetracoordinate $1\lambda^4$,2-thiazetidine. The Martin ligand was used to stabilize these sulfuranes.[7]

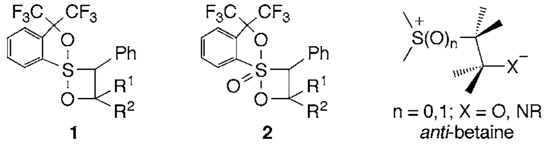
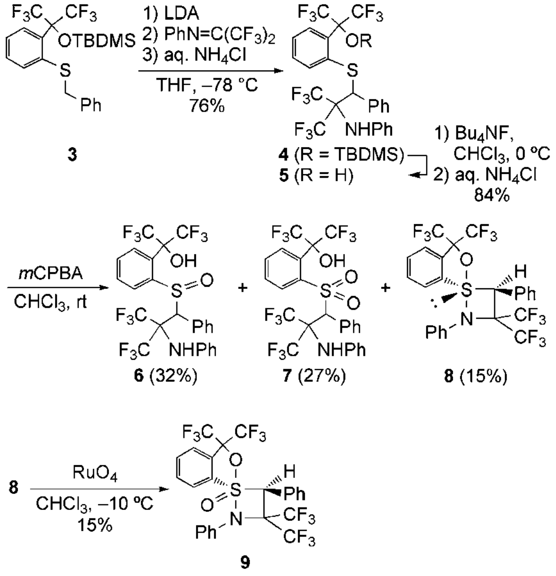


Figure 1. Tetracoordinate and pentacoordinate 1,2-oxathietanes **1** and **2** and *anti*-betaines.

Sequential treatment of benzyl sulfide **3**[6d] with lithium diisopropylamide (2.2 equiv), (hexafluoroisopropylidene)-aniline (1.1 equiv), and an aqueous solution of NH_4Cl gave β-aminoalkyl sulfide **4** (76%), which was converted to **5** with $(n\text{-Bu})_4NF$ (0.84 equiv) (84%) (Scheme 1). The oxidation of **5** with *m*-CPBA (2.0 equiv) in chloroform gave sulfoxide **6** (32%), sulfone **7** (27%), and tetracoordinate $1\lambda^4$,2-thiazetidine **8** (15%). Compounds **6** and **8** were obtained as a single diastereomer, although the stereochemistry of **6** has not been determined. Oxidation of **8** with 4.0 equiv of RuO_4 in CCl_4 at room temperature gave the corresponding oxidized product, pentacoordinate 1,2-thiazetidine **9** (15%), with recovery of **8** (74%).[11] Either prolonged stirring or heating at higher temperatures in the last reaction resulted in the formation of unidentified byproducts, which made it difficult to separate **9** cleanly.

Scheme 1. Syntheses of 1,2-Thiazetidines **8** and **9**



The molecular structures of **8** (Supporting Information) and **9** (Figure 2) were established by X-ray crystallographic analyses.[12] Compounds **8** and **9** are the first examples of the syntheses and structural analyses of a tetracoordinate $1\lambda^4$,2-thiazetidine and a pentacoordinate $1\lambda^6$,2-thiazetidine, respectively. The molecular structure of **9** was found to be distorted

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(12) Crystal data of **9**: $C_{25}H_{15}F_{12}NO_2S$, FW = 621.44, colorless crystals, orthorhombic, space group $Pna2_1$, $a = 10.371(4)$ Å, $b = 16.811(7)$ Å, $c = 14.108(6)$ Å, $V = 2459.7(18)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.678$ g cm^{-3}, $T = 110(2)$ K, $R1(I > 2\sigma(I)) = 0.0243$ and wR2(all data) = 0.0572.

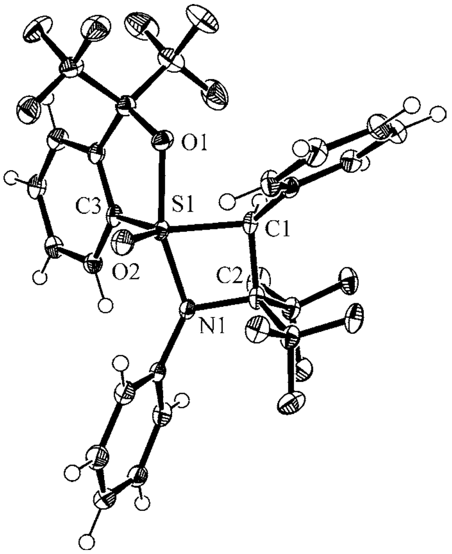
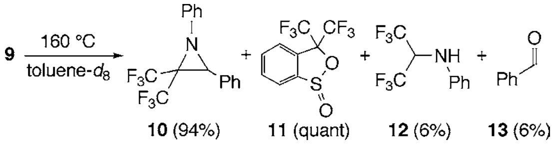


Figure 2. ORTEP drawing of **9** with thermal ellipsoids plot (50% probability). Selected bond lengths (Å), angles (deg), and torsion angles (deg) for **9**: S1−N1, 1.7751(15); S1−C1, 1.8455(17); C1−C2, 1.556(3); C2−N1, 1.455(2); S1−O1, 1.8383(14); S1−O2, 1.4476(14); S1−C3, 1.7930(19); C1−S1−N1, 75.75(8); S1−C1−C2, 90.91(11); C1−C2−N1, 95.11(13); C2−N1−S1, 97.22(11); O1−S1−N1, 159.42(6); C1−S1−C3, 119.09(8); C1−S1−O2, 125.96(9); O2−S1−C3, 114.74(8); S1−N1−C2−C1, 8.42(12); S1−C1−C2−N1, 8.03(12).

trigonal bipyramidal structures at a sulfur atom with O1 and N1 atoms at apical positions and with C1, C3, and O2 atoms at equatorial positions. The bond angle of two apical bonds of **9** deviates by 20.58(6)° from 180°, due to their ring strain. Configuration on the central sulfur atom in **8** and **9** indicates that oxidation of **8** proceeded with retention of configuration. The S1−N1 bond length of **9** (1.7751(15) Å) is somewhat longer than those of β-sultams (1.638−1.698 Å)[13] and the sum of the corresponding covalent radii (1.74 Å)[14] because of the hypervalency. The equatorial S1−O2 bond length of **9** (1.4476(14) Å) is similar to that of the previously reported sulfurane oxides (1.439(4)-1.445(6) Å).[6c,10] The 1,2-thiazetidine ring of **9** deviates from planarity, as indicated by their S1−N1−C2−C1 torsion angle [8.42(12)°].

On one hand, thermolysis of tetracoordinate $1\lambda^4$,2-thiazetidine **8** at 210 °C in *o*-xylene-d_{10} for 81 h gave a complex mixture, and most of the products could not be identified, in contrast to thermolysis of the corresponding selenium analogue.[6g] On the other hand, thermolysis of the pentacoordinate $1\lambda^6$,2-thiazetidine **9** gave a clear result. Upon heating at 160 °C in toluene-d_8 for 17 h, pentacoordinate 1,2-thiazetidine **9** afforded the corresponding aziridine **10** (94%), the cyclic sulfinate **11** (100%), amine **12** (6%), and benzaldehyde (**13**) (6%) (Scheme 2).[15] No formation of the corresponding olefin was observed. The latter two compounds, **12** and **13**, must be formed by the hydrolysis of aziridine **10**. That is, the result shows the almost quantitative formation of aziridine **10** and cyclic sulfinate **11** in the thermolysis of **9**. Considering that the oxygen analogue of **9**, pentacoordinate $1,2\lambda^6$-oxathietanes **1**, gave the corresponding oxirane[6] and that the selenium analogue of **8**, a tetracoordinate $1,2\lambda^4$-selenazetidine, gave the corresponding aziridine,[6g] the results show that the pentacoordinate 1,2-thiazetidine has a similar reactivity to them at the point of formation of the corresponding three-membered ring compound on thermolysis.

Scheme 2. Thermolysis of **9**



A pentacoordinate $1\lambda^6$,2-thiazetidine can be regarded as a [2 + 2]-cycloadduct of the polarized $C^-{-}S^+$ bond of an oxosulfonium ylide to the C═N bond of an imine. Formation of the aziridine from 1,2-thiazetidine **9** suggests that a pentacoordinate $1,2\lambda^6$-thiazetidine might be an intermediate of the aziridine formation reaction from an oxosulfonium ylide with an imine, i.e., the aza-Corey−Chaykovsky reaction.[3e]

In summary, we have not only succeeded in the first synthesis and isolation of both a tetracoordinate $1,2\lambda^4$-thiazetidine and a pentacoordinate $1,2\lambda^6$-thiazetidine but also proved the aziridine formation from the $1,2\lambda^6$-thiazetidine. These experimental results suggest the participation of the $1,2\lambda^6$-thiazetidine as a transition state or an intermediate in the aza-Corey−Chaykovsky reaction of an oxosulfonium ylide. A study of the stereochemistry of the aziridine formation reaction from a $1,2\lambda^6$-thiazetidine and its reaction pathway is in progress.

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Supporting Information Available: Synthetic procedures and spectral data for **4**−**9**; X-ray crystallographic files for **8** and **9** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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