ORGANIC
LETTERS

2006
Vol. 8, No. 20
4625−4627

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

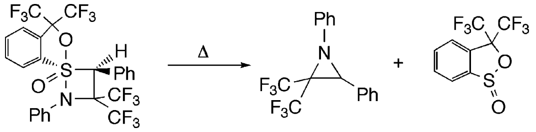
Naokazu Kano, Yuya Daicho, and Takayuki Kawashima*

Department of Chemistry, Graduate School of Science, The University of Tokyo,
7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

takayuki@chem.s.u-tokyo.ac.jp

Received July 26, 2006

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

---

(1) (a) Johnson, A. W.; LaCount, R. B. *J. Am. Chem. Soc.* **1961**, *83*, 417−423. (b) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1962**, *84*, 3782−3783. (c) Durst, T.; Viau, R.; Van Den Elzen, R.; Nguyen, C. H. *J. Chem. Soc., Chem. Commun.* **1971**, 1334−1336. (d) Johnson, C. R.; Schroeck, C. W. *J. Am. Chem.* Soc. **1971**, *93*, 5303−5305. (e) Townsend, J. M.; Sharpless, K. B. *Tetrahedron Lett.* **1972**, 3313−3316. (f) Trost, B. M.; Meiwin, L. S., Jr. In *Sulfur Ylides, Emerging Sythetic Intermediates*; Academic Press: New York, 1975. (g) Aubé, J. In *Comprehensive Organic Synthesis: Selectivity, Strategy, and Efficiency in Modern Synthetic Chemistry*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 1, pp 822−825.

(2) (a) Franzen, V.; Driesen, H.-E. *Chem. Ber.* **1963**, *96*, 1881−1890. (b) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353−1364. (c) Hortmann, A. G.; Robertson, D. A. *J. Am. Chem. Soc.* **1967**, *89*, 5974−5975. (d) Tewari, R. S.; Awasthi, A. K.; Awasthi, A. *Synthesis* **1983**, 330−331. (e) Mosset, P.; Gree, R. *Synth. Commun.* **1985**, *15*, 749−757. (f) Li, A.-H.; Dai, L.-X.; Hou, X.-L. *Chem. Commun.* **1996**, 491−492. (g) Li, A.-H.; Dai, L.-X.; Hou, X.-L. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2725−2729. (h) Li, A.-H.; Dai, L.-X.; Hou, X.-L.; Chen, M.-B. *J. Org. Chem.* **1996**, *61*, 4641−4648. (i) Zhou, Y.-G.; Li, A.-H.; Hou, X.-L.; Dai, L.-X. *Tetrahedron Lett.* **1997**, *38*, 7225−7228. (j) Hou, X.-L.; Yang, X.-F.; Dai, L.-X.; Chen, X.-F. *Chem. Commun.* **1998**, 747−748. (k) Deng, W.-P.; Li, A.-H.; Dai, L.-X.; Hou, X.-L. *Tetrahedron* **2000**, *56*, 2967−2974. (l) Saito, T.; Sakairi, M.; Akiba, D. *Tetrahedron Lett.* **2001**, *42*, 5451−5454. (m) Aggarwal, V. K.; Ferrara, M.; O'Brien, C. J.; Thompson, A.; Jones, R. V. H.; Fieldhouse, R. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1635−1643.

(3) (a) Johnson, C. R. *Acc. Chem. Res.* **1973**, *6*, 341−347. (b) Johnson, C. R.; Schroeck, C. W.; Shanklin, J. R. *J. Am. Chem. Soc.* **1973**, *95*, 7424−7431. (c) Ruano, J. L. G.; Fernández, I.; Hamdouchi, C. *Tetrahedron Lett.* **1995**, *36*, 295−298. (d) Davis, F. A.; Zhou, P.; Liang, C.-H.; Reddy, R. E. *Tetrahedron: Asymmetry* **1995**, *6*, 1511−1514. (e) Ruano, J. L. G.; Fernández, I.; Catalina, M. D. P.; Cruz, A. A. *Tetrahedron: Asymmetry* **1996**, *7*, 3407−3414. (f) Osborn, H. M. I.; Sweeney, J. *Tetrahedron: Asymmetry* **1997**, *8*, 1693−1715. (g) Zhu, W.; Li, Y.; Chen, Z.; Li, D.; Yang, G. *Synth. Commun.* **2000**, *30*, 1075−1081.

(4) Wang, D.-K.; Dai, L.-X.; Hou, X.-L. *Chem. Commun.* **1997**, 1231−1232.

(5) (a) Aggarwal, V. K.; Thompson, A.; Jones, R. V. H.; Standen, M. C. H. *J. Org. Chem.* **1996**, *61*, 8368−8369. (b) Aggarwal, V. K.; Vasse, J.-L. *Org. Lett.* **2003**, *5*, 3987−3990.

10.1021/ol0618499 CCC: $33.50

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 1λ^6,2-thiazetidine, a novel type of sulfurane oxide.[6c,10] We also discuss its comparison with a tetracoordinate 1λ^4,2-thiazetidine. The Martin ligand was used to stabilize these sulfuranes.[7]

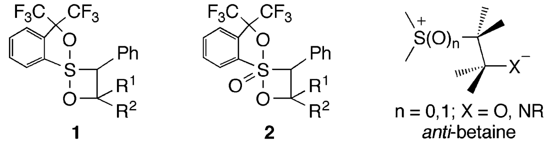
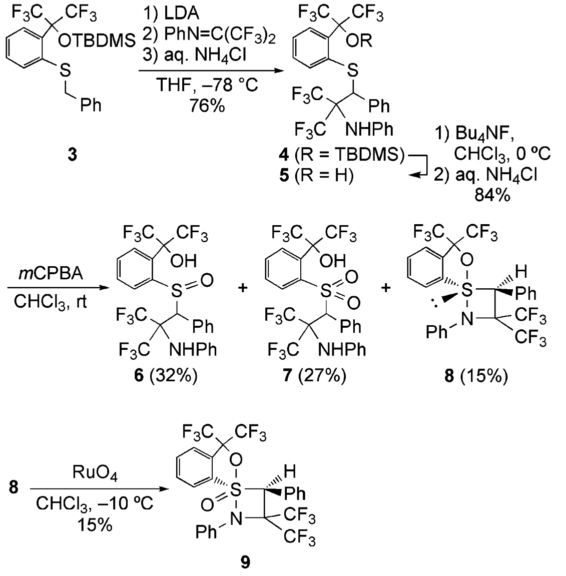


Figure 1. Tetracoordinate and pentacoordinate 1,2-oxathietanes **1** and **2** and *anti*-betaines.

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 1λ^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 1λ^4,2-thiazetidine and a pentacoordinate 1λ^6,2-thiazetidine, respectively. The molecular structure of **9** was found to be distorted

---

[6] (a) Kawashima, T.; Ohno, F.; Okazaki, R. *J. Am. Chem. Soc.* **1993**, *115*, 10434−10435. (b) Kawashima, T.; Ohno, F.; Okazaki, R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2094−2095. (c) Ohno, F.; Kawashima, T.; Okazaki, R. *J. Am. Chem.* Soc. **1996**, *118*, 697−698. (d) Kawashima, T.; Ohno, F.; Okazaki, R.; Ikeda, H.; Inagaki, S. *J. Am. Chem. Soc.* **1996**, *118*, 12455−12456. (e) Ohno, F.; Kawashima, T.; Okazaki, R. *Chem. Commun.* **1997**, 1671−1672. (f) Ohno, F.; Kawashima, T.; Okazaki, R. *Chem. Commun.* **2001**, 463−464. (g) Kano, N.; Daicho, Y.; Nakanishi, N.; Kawashima, T. *Org. Lett.* **2001**, *3*, 691−694. (h) Kano, N.; Takahashi, T.; Kawashima, T. *Tetrahedron Lett.* **2002**, *43*, 6775−6778. (i) Kawashima, T. *Coord. Chem. Rev.* **2003**, *244*, 137−147.

[7] Perozzi, E. F.; Michalak, R. S.; Figuly, G. D.; Stevenson, W. H., III; Dess, D. B.; Ross, M. R.; Martin, J. C. *J. Org. Chem.* **1981**, *46*, 1049−1053.

[8] (a) Li, A.-H.; Zhou, Y.-G.; Dai, L.-X.; Hou, X.-L.; Xia, L.-J.; Lin, L. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1317−1319. (b) Li, A.-H.; Zhou, Y.-G.; Dai, L.-X.; Hou, X.-L.; Xia, Li-J.; Lin, L. *J. Org. Chem.* **1998**, *63*, 4338−4348.

[9] (a) Timberlake, J. W.; Elder, E. S. In *Comprehensive Heterocyclic Chemistry*; Lwowski, W., Vol. Ed.; Pergamon Press: Oxford, 1984; Vol. 7, Chapter 5.15. (b) Harris, P. A. In *Comprehensive Heterocyclic Chemistry II*; Padwa, A., Vol. Ed.; Pergamon Press: Oxford, 1996; Vol. 1, Chapter 1.32. (c) Otani, T.; Takayama, J.; Sugihara, Y.; Ishii, A.; Nakayama, J. *J. Am. Chem. Soc.* **2003**, *125*, 8255−8263. (d) Page, M. I. *Acc. Chem. Res.* **2004**, *37*, 297−303.

[10] (a) Martin, J. C.; Perozzi, E. F. *J. Am. Chem. Soc.* **1974**, *96*, 3155−3168. (b) Perrozi, E. F.; Martin, J. C.; Paul, I. C. *J. Am. Chem. Soc.* **1974**, *96*, 6735−6744. (c) Adzima, L. J.; Martin, J. C. *J. Am. Chem. Soc.* **1977**, *99*, 1657−1659. (d) Lau, P. H. W.; Martin, J. C. *J. Am. Chem. Soc.* **1977**, *99*, 5490−5491. (e) Rongione, J. C.; Martin, J. C. *J. Am. Chem. Soc.* **1990**, *112*, 1637−1638.

[11] Perozzi, E. F.; Martin, J. C. *J. Am. Chem. Soc.* **1972**, *94*, 5519−5520.

[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 $wR2(\text{all data}) = 0.0572$.

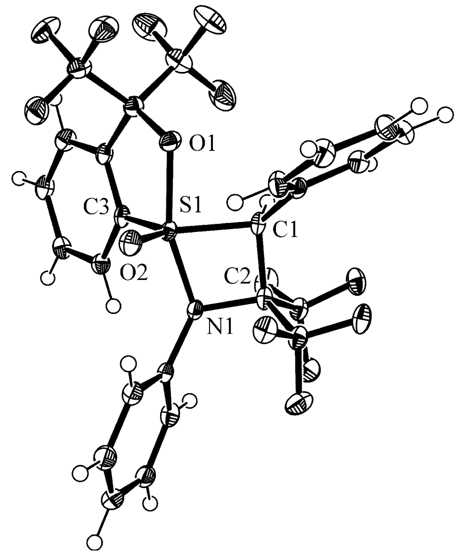
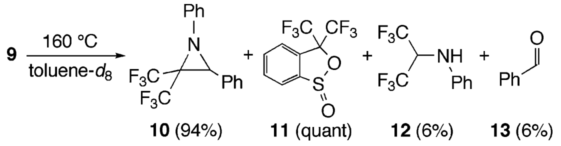


Figure 2. ORTEP drawing of **9** with thermal ellipsoids plot (50% probability). Selected bond lengths (Å), angles (deg), and torsion angles (deg) for **9**: S1−N1, 1.7751(15); S1−C1, 1.8455(17); C1−C2, 1.556(3); C2−N1, 1.455(2); S1−O1, 1.8383(14); S1−O2, 1.4476(14); S1−C3, 1.7930(19); C1−S1−N1, 75.75(8); 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.

Acknowledgment. We thank Central Glass, Shin-etsu Chemical Co., Ltd., and Tosoh Finechem Corp. for the gifts of organofluorine compounds, organosilicon compounds, and alkyllithiums, respectively. We also thank the Ministry of Education, Culture, Sports, Science and Technology of Japan for financial support.

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.

OL0618499

---

(13) (a) Chiaroni, A.; Riche, C.; Loiseau, P.; Bonnafous, M.; Adam, Y. *Acta Crystallogr. Sect. C* **1985**, *41*, 1265−1267. (b) Meyle, E.; Keller, E.; Otto, H.-H. *Liebigs Ann. Chem.* **1985**, 802−812. (c) Belskii, V. K.; Bodrikov, I. V.; Michurin, A. A.; Chumakova, L. I.; Zhivoderov, A. V. *Tetrahedron Lett.* **1985**, *26*, 5689−5692. (d) Meyle. E.; Otto, H.-H.; Kratky, C. *Monatsch. Chem.* **1985**, *116*, 493−503. (e) Michurin, A. A.; Bodrikov, I. V.; Bel'skii, V. K.; Titova, O. M.; Zhivoderov, A. V. *Zh. Org. Khim.* **1988**, *24*, 1978−1987. (f) Mueller, M.; Meyle, E.; Paulus, E. F.; Plagge, H.; Otto, H.-H. *Liebigs Ann. Chem.* **1989**, 975−983. (g) Mihova, T. R.; Linden, A.; Heimgartner, H. *Helv. Chim. Acta* **1996**, *79*, 2067−2074. (h) Glasl, D.; Rihs, G.; Otto, H.-H. *Helv. Chim. Acta* **1997**, *80*, 671−683. (i) Iwama, T.; Kataoka, T.; Muraoka, O.; Tanabe, G. *J. Org. Chem.* **1998**, *63*, 8355−8360. (j) Todorova, T. R.; Linden, A.; Heimgartner, H. *Helv. Chim. Acta* **1999**, *82*, 354−371. (k) Baldoli, C.; Del Buttero, P.; Perdicchia, D.; Pilati, T. *Tetrahedron* **1999**, *55*, 14089−14096.

(14) Pauling, L. In *The Nature of the Chemical Bond*, 3rd ed.; Cornell University Press: New York, 1960; p 246.

(15) The yields of these products were determined on the basis of the integral of ^{1}H and ^{19}F NMR spectra of the reaction solution.