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Acidic and Basic Hydrolysis of an Optically Pure Spiro-λ^4-sulfurane: Completely Opposite Stereochemical Outcome

Jian Zhang, Shinichi Saito, and Toru Koizumi*[†]

Faculty of Pharmaceutical Sciences
Toyama Medical & Pharmaceutical University
2630 Sugitani, Toyama 930-01, Japan

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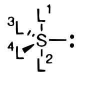
Sulfurane (**1**) has been proposed as an intermediate in various reactions of organosulfur compounds.[1] A number of achiral sulfuranes have been prepared, and the structural as well as the chemical properties were investigated.[2] However, the stereochemistry of chiral sulfuranes and stereochemical process of their reactions have been scarcely studied.[3,4] We designed a series of chiral alkoxyacyloxyspirosulfuranes using the 2-*exo*-hydroxy-10-bornyl group as a chiral ligand to study the stereochemistry of sulfuranes and their reactions. Herein we report the synthesis, structural determination and the mechanistic research on the hydrolysis of optically pure spirosulfuranes.



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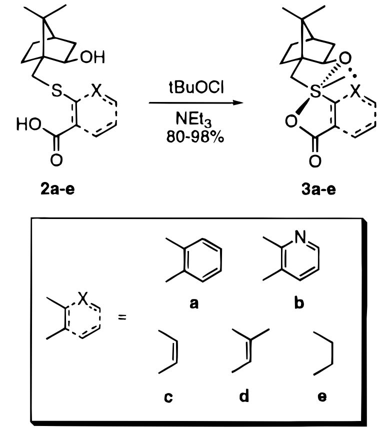
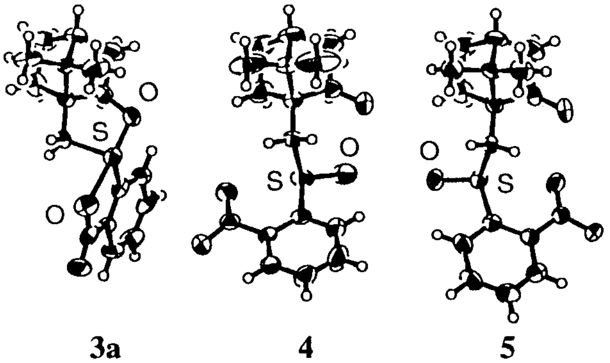
We synthesized the chiral spiro-λ^4-sulfuranes (**3a**−**e**) as illustrated in Scheme 1.[5] Spirosulfuranes (**3a**−**d**) were obtained as colorless crystals in high yield and as single diastereomers. An X-ray crystallographic analysis of **3a** indicated that the spirosulfuranes have a slightly distorted trigonal bipyramidal (TBP) structure as shown in Figure 1.[6]

To give a deep insight into the stereochemistry of the nucleophilic reactions of hypervalent sulfur compounds and how the coordinated groups bound to the sulfur atom affect this process, we carried out the hydrolysis of spirosulfurane (**3a**) under various conditions (Scheme 2 and Table 1). Compound **3a** was easily hydrolyzed under a basic condition (1 N NaOH) to give optically pure sulfoxide (**4**) as a single diastereomer (Table 1, entry 1). The (*R*) absolute configuration of the sulfur atom in sulfoxide (**4**) has been determined by an X-ray analysis (Figure 1).[7] *In contrast, hydrolysis of spirosulfurane (3a) under an acidic condition (1 N HCl) gave sulfoxide (5), also as a single diastereomer but with an opposite absolute configuration at the sulfur atom* (Table 1, entry 2). The stereochemistry of sulfoxide (**5**) was also clearly determined by an X-ray analysis (Figure 1).[8]

Scheme 1

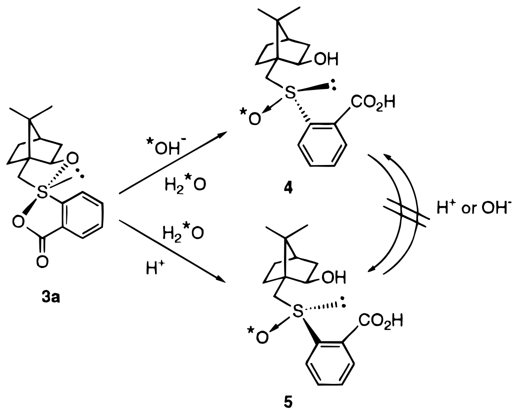




3a **4** **5**

Figure 1. ORTEP drawings of the compounds **3a**, **4**, and **5** with 50% thermal ellipsoids.

Scheme 2



Next, we confirmed that the sulfoxides did not isomerize under the conditions employed for the hydrolysis. Stirring the sulfoxides (**4** or **5**) under basic or acidic conditions afforded only the starting materials (Table 1, entries 3−6).[8] These results clearly rule out the possibility of pH-dependent isomerization of these sulfoxides, and we, therefore, conclude that the chiral sulfoxides obtained here are stereoselectively formed by the hydrolysis.

[†] Deceased, January 12, 1998.

(1) Martin, J. C.; Paul, I. C. *Science* **1976**, *191*, 154−159.

(2) (a) Kapovits, I.; Kálmán, A. *J. Chem. Soc., Chem. Commun.* **1971**, 649−650. (b) Adzima, L. J.; Martin, J. C. *J. Org. Chem.* **1977**, *42*, 4006−4016. (c) Kapovits, I.; Rábai, J.; Szabó, D.; Czakó, K.; Kucsman, Á.; Argay, G.; Fülöp, V.; Kálmán, A.; Koritsánszky, T.; Párkányi, L. *J. Chem. Soc., Perkin Trans. 2* **1993**, 847−853. (d) Vass, E.; Ruff, F.; Kapovits, I.; Rábai, J.; Szabó, D. *J. Chem. Soc., Perkin Trans. 2* **1993**, 855−859. (e) Hornbuckle, S. F.; Livant, P.; Webb, T. R. *J. Org. Chem.* **1995**, *60*, 4153−4159. (f) Rabai, J.; Kapovits, I.; Argay, G.; Koritsanszky, T.; Kalman, A. *J. Chem. Soc., Chem. Commun.* **1995**, 1069−1070. (g) Szabó, D.; Kapovits, I.; Argay, G.; Czugler, M.; Kálmán, A.; Koritsánszky, T. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1045−1053.

(3) (a) Huszthy, P.; Kapovits, I.; Kucsman, Á.; Radics, L. *Tetrahedron Lett.* **1978**, 1853−1856. (b) Allenmark, S.; Claeson, S. *Tetrahedron: Asymmetry* **1993**, *4*, 2329−2332. (c) Drabowicz, J.; Martin, J. C. *Tetrahedron: Asymmetry* **1993**, *4*, 297−300. (d) Drabowicz, J.; Martin, J. C. *Pure Appl. Chem.* **1996**, *68*, 951−956. (e) Szabó, D.; Szendeffy, S.; Kapovits, I.; Kucsman, Á.; Czugler, M.; Kálmán, A.; Nagy, P. *Tetrahedron: Asymmetry* **1997**, *8*, 2411−2420.

(4) Zhang, J.; Takahashi, T.; Koizumi, T. *Heterocycles* **1997**, *44*, 325−339, and references therein.

(5) See Supporting Information for detailed procedures. The structure of sulfurane (**3e**) was determined by the ^{1}H NMR analysis of the crude product since it is not stable to moisture.

(6) Crystal data for **3a**: $C_{17}H_{20}SO_3$, colorless crystal, MW = 304.40, orthorhombic, space group $P2_12_12_1$ (#19) with $a = 11.206(3)$ Å, $b = 12.282(2)$ Å, $c = 10.965(3)$ Å, $V = 1509.1(5)$ Å^3, $Z = 4$, density(calcd) = 1.34 g cm^{-3}, $F(000) = 648.00$, $\lambda = 0.710\,69$ Å, $T = 293$ K, μ (Mo Kα) = 2.22 cm^{-1}. Intensity data were collected on a Rigaku AFC7R diffractometer using a 0.15 × 0.15 × 0.20 mm^3 sized crystal. 1999 unique reflections; 766 with $I > 3.00\sigma(I)$ were used in refinement; $R = 4.2\%$, $R_w = 4.4\%$.

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Table 1. The Reaction of **3a**, **4**, and **5** under Basic or Acidic Conditions

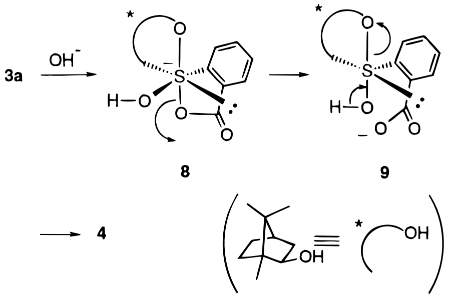
entry	substrate	condition	product[a]	yield (%)
1	**3a**	1 N NaOH, 0 °C, 0.5 h	**4**	88
2	**3a**	1 N HCl, rt,[b] 48 h	**5**	98
3	**4**	1 N NaOH, rt,[b] 48 h	**4**	92
4	**4**	1 N HCl, rt,[b] 48 h	**4**	98
5	**5**	1 N NaOH, rt,[b] 48 h	**5**	96
6	**5**	1 N HCl, rt,[b] 48 h	**5**	98

[a] No isomer was detected by an ^{1}H NMR analysis. [b] Room temperature = rt.

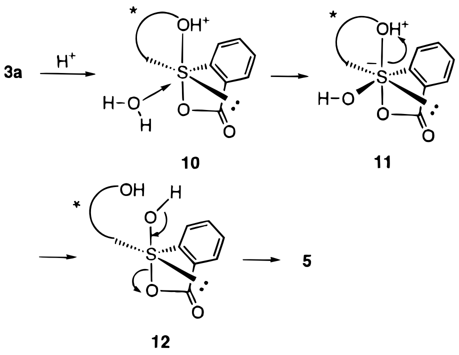
Finally, we performed the hydrolysis of spirosulfurane (**3a**) with isotopically labeled H_2O to see whether and where the oxygen atom of H_2O attack the spirosulfurane. Spirosulfurane (**3a**) was hydrolyzed under basic or acidic conditions in the presence of $H_2{}^{18}O$ (97 atom % ^{18}O) followed by treatment with diazomethane to give methyl esters **6-^{18}O** and **7-^{18}O**.[9] Mass spectroscopic analyses revealed that **6-^{18}O** and **7-^{18}O** are enriched with ^{18}O to a significant extent (70% and 91% incorporation, respectively).[9] On the other hand, the sulfoxides (**4-^{17}O** and **5-^{17}O**) obtained by hydrolysis of **3a** with $H_2{}^{17}O$ (20.3 atom % ^{17}O) under basic or acidic conditions showed signals with chemical shift of −9.2 and −8.1 ppm in their ^{17}O NMR spectra, respectively. The values of the chemical shift strongly indicate that under both conditions the oxygen atoms from $H_2{}^{17}O$ were bound to the sulfur atoms.[10] Based on these results, we concluded that the oxygen of H_2O attacked sulfur atom directly in the hydrolysis.

We propose the mechanism of these reactions as follows: hydrolysis under basic condition may proceed through the attack of hydroxide ion onto the central sulfur atom to give an intermediate (**8**) (Scheme 3).[11] Cleavage of S−O (acyloxy) bond[12] and isomerization around the sulfur center generates the pentacoordinate intermediate (**9**) with the hydroxyl group at the apical position.[13] Then, deprotonation and tandem breaking of the S−O (alkoxy) bond takes place to give the highly diastereoselective formation of the sulfoxide (**4**) with *R* absolute configuration.

Scheme 3



Scheme 4



Under the acidic condition, the reaction may proceed through the initial protonation of the spirosulfurane at the oxygen of alkoxy,[14] then attack of H_2O to the sulfur atom takes place, and a hexacoordinate sulfur intermediate (**11**) is formed (Scheme 4). Cleavage of the S−O (alkoxy) bond of the intermediate (**11**) and isomerization around the sulfur center produce an intermediate (**12**) with the hydroxyl group at the apical position.[13] Final deprotonation and consecutive breaking of the S−O (acyloxy) bond gave sulfoxide (**5**) with *S* absolute configuration at the sulfur atom.[15]

In summary, an optically pure sulfurane (**3a**) was stereoselectively hydrolyzed under basic and acidic conditions to give the sulfoxides (**4** and **5**) with the completely opposite absolute configuration at sulfur atom. We proposed the mechanism of the reaction which accounts for the observed stereochemical outcome. The results obtained here would be helpful for the understanding of the stereochemistry of the nucleophilic reaction concerning the hypervalent compounds.

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Supporting Information Available: Detailed synthetic procedures and spectroscopic data for sulfides and compounds **3a**−**e**, **4**, **5**, **6**, and **7** and structure determination summary and listings of final atomic coordinates, thermal parameters, bond lengths, and bond angles for compounds **3a**, **4**, and **5** (67 pages). See any current masthead page for ordering and Web access instructions.

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(7) Crystal data for **4**: $C_{17}H_{22}SO_4$, colorless crystal, MW = 322.42, orthorhombic, space group $P2_12_12_1$ (#19) with a = 13.124(3) Å, b = 14.720(3) Å, c = 8.659(2) Å, V = 1672.8(5) Å^3, Z = 4, density(calcd) = 1.280 g cm^{-3}, F(000) = 688.00, λ = 0.710 69 Å, T = 293 K, μ (Mo Kα) = 2.08 cm cm^{-1}. Intensity data were collected on a Rigaku AFC7R diffractometer using a 0.20 × 0.20 × 0.25 mm^3 sized crystal. 2216 unique reflections; 1464 with $I > 3.00\sigma(I)$ were used in refinement; R = 4.2%, R_w = 4.1%. Crystal data for **5**: $C_{17}H_{22}SO_4$, colorless crystal, MW = 322.42, monoclinic, space group $P2_1$ (#4) with a = 6.961(4) Å, b = 10.993(3) Å, c = 10.765(4) Å, β = 103.04(4)°, V = 802.6(6) Å^3, Z = 2, density(calcd) = 1.334 g cm^{-3}, F(000) = 344.00, λ = 0.710 69 Å, T = 293 K, μ (Mo Kα) = 2.17 cm^{-1}. Intensity data were collected on a Rigaku AFC7R diffractometer using a 0.30 × 0.20 × 0.20 mm^3 sized crystal. 2084 unique reflections; 1138 with $I > 3.00\sigma(I)$ were used in refinement; R = 4.1%, R_w = 4.2%.

(8) Refluxing the sulfoxides (**4** or **5**) under basic condition for 5 h gave also the starting material recovered. Slight isomerization was observed when the sulfoxides (**4** or **5**) were refluxed in 1 N HCl−EtOH.

(9) Esterification was necessary in order to observe the mass spectra. The isotopic purity is calculated by comparing the height of peaks at m/z = 186 [(M^+− ^{18}**O**) − $C_{10}H_{16}O$] with that of peaks at m/z = 184 [(M^+ − ^{16}**O**) − $C_{10}H_{16}O$] in the mass spectra of sulfoxides (**6-^{18}O** or **7-^{18}O**), while in the mass spectra of sulfoxides (**6-^{16}O** or **7-^{16}O**) there are no peaks at m/z = 186.

(10) (a) Boykin, D. W.; Baumstark, A. L. *Tetrahedron* **1989**, *45*, 3613−3651. (b) Dyer, J. C.; Harris, D. C.; Evans, J. S. A. *J. Org. Chem.* **1982**, *47*, 3660−3664.

(11) Martin, J. C.; Balthazor, T. M. *J. Am Chem. Soc.* **1977**, *99*, 152−162.

(12) The S−O (acyloxy) bond is expected to be hydrolyzed easier compared to the S−O (alkoxy) bond. See: Lam, W. Y.; Duesler, E. N.; Martin, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 127−135.

(13) The pentacoordinated intermediates (**9** and **12**) can be reasonably considered as with the TBP geometries and the most electronegative groups in **9** and **12** are expected to occupy axial positions.

(14) The basicity of ethers (p$K_{BH}{}^+$ = −3.5) is generally stronger than that of esters (p$K_{BH}{}^+$ = −6.5). March, J. *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure;* Wiley-Interscience: New York, 1992; p 250.

(15) Alternatively, the cleavage of the S−O (alkoxy) bond may be induced by the initial protonation to give a sulfonium cation, then the attack of water onto the sulfur atom from pseudoaxial direction may afford the intermediate (**12**).