Isolation and Stereochemical Studies of a Cyclic Alkoxysulfonium Salt, an Important Intermediate in the Nucleophilic Reaction of Chlorooxasulfuranes

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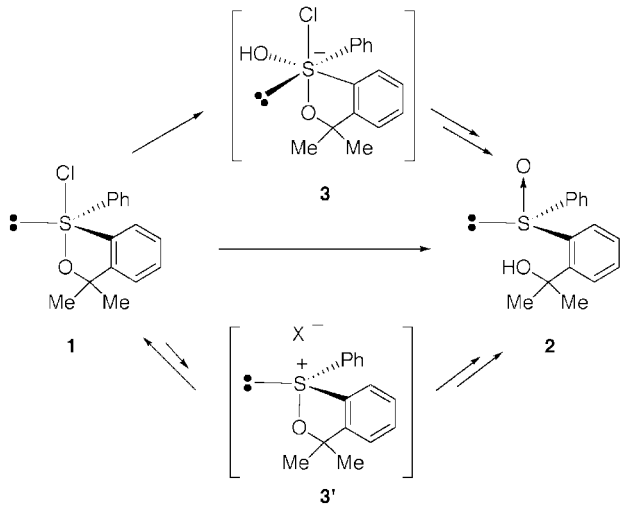
The stereochemical research on the nucleophilic reaction of compounds at a tetracoordinated atom, such as carbon, has been widely carried out, and the S_N1 or S_N2 pathway has been accepted as the general concept of organic reactions. In contrast, the study of the stereochemical process of the nucleophilic reaction of the hypervalent compounds has been carried out to a much lesser extent. Chalcogenurane, a pentacoordinated hypervalent compound, usually adopts a trigonal-bipyramidal geometry. The stereochemical study on the reaction of chalcogenurane would lead to the understanding of the general mechanism of the reactions occurring at a multicoordinated heteroatom. However, since the lack of optically pure chalcogenurane, few studies have been reported in this field. Twenty years ago, Martin et al. studied the mechanism of the basic hydrolysis of chiral chlorosulfurane **1** to give sulfoxide **2** and proposed an associative mechanism involving a hexacoordinated sulfur species **3** with a negative charge on sulfur (Scheme 1).[1] They also reported the isolation and hydrolysis of chiral sulfonium salt **3′** ($X = BF_4^-$) during their research. However, the absolute configuration of the sulfonium salt **3′** and the chlorosulfurane **1** was indirectly confirmed, and the stereochemical relationship between the sulfonium salt and chlorosulfurane as well as the mechanism of the reaction remains to be clearly established.

We have carried out the synthesis, reaction, and stereochemical research on the chiral hypervalent chalcogenium compounds and assumed that the chiral chalcogenonium cations **4** would be an intermediate in some reactions (Scheme 2).[2] In this paper we report the isolation, stereochemistry, and hydrolysis of a chiral alkoxysulfonium salt which has been proposed as an intermediate in the hydrolysis of chlorosulfuranes.[3]

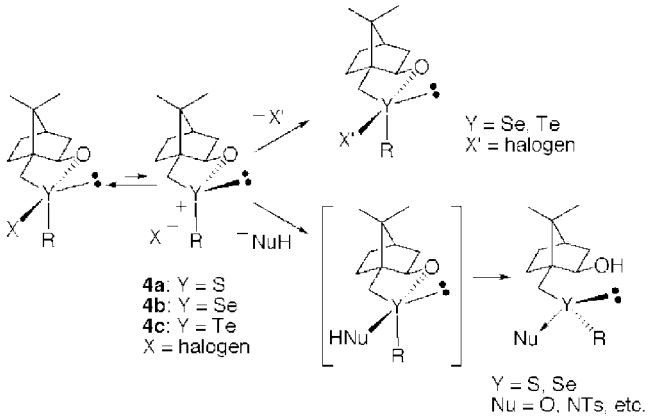
Reaction of sulfide **5** with *t*-BuOCl (1.1 equiv) at 0 °C for 20 min in anhydrous dichloromethane under nitrogen atmosphere gave chlorooxasulfurane **6** as a white solid after evaporation of the solvent and excess reagents.[3] The stereochemistry of **6** was determined by comparing the spectroscopic data of **6** with those of a selenium analogue.[2e] Reaction of chlorosulfurane **6** with AgF at 0 °C for 30 min afforded fluorosulfurane **7** as the sole product via halogen-exchange reaction. It is likely that the reaction proceeds via an S_N1 pathway which involves a sulfonium cation as an intermediate (Scheme 3).[2f]

To isolate the cationic intermediate, chlorosulfurane **6** was treated with silver tetrafluoroborate (1.1 equiv) to give optically pure alkoxysulfonium salt **8** in 96% yield and as a single diastereomer (Scheme 3).[5] Other epimeric compounds were not detected. The salt **8** was characterized by spectroscopic means. In the ^1H NMR spectrum, the signals of methylene protons (H_a, H_b) of **8** appeared

Scheme 1



Scheme 2



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(1) (a) Balthazor, T. M.; Martin, J. C. *J. Am. Chem. Soc.* **1975**, *97*, 5634−5635. (b) Martin, J. C.; Balthazor, T. M. *J. Am. Chem. Soc.* **1977**, *99*, 152−162.

(2) (a) Takahashi, T.; Kurose, N.; Kawanami, S.; Arai, Y.; Koizumi, T.; Shiro, M. *J. Org. Chem.* **1994**, *59*, 3262−3264. (b) Takahashi, T.; Kurose, N.; Kawanami, S.; Nojiro, A.; Arai, Y.; Koizumi, T.; Shiro, M. *Chem. Lett.* **1995**, 379−380. (c) Kurose, N.; Takahashi, T.; Koizumi, T. *J. Org. Chem.* **1996**, *61*, 2932−2933. (d) Takahashi, T.; Zhang, J.; Kurose, N.; Takahashi, S.; Koizumi, T.; Shiro, M. *Tetrahedron: Asymmetry* **1996**, *7*, 2797−2800. (e) Kurose, N.; Takahashi, T.; Koizumi, T. *Tetrahedron* **1997**, *53*, 12115−12129. (f) Takahashi, S.; Zhang, J.; Saito, S.; Koizumi, T. *Heterocycles* **1997**, *46*, 373−384. (g) Zhang, J.; Saito, S.; Koizumi, T. *Tetrahedron: Asymmetry* **1997**, *8*, 3357−3361.

(3) Zhang, J.; Takahashi, T.; Koizumi, T. *Heterocycles* **1997**, *44*, 325−339.

(4) For the reactions involving sulfonium salts, see: (a) Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 164−185. (b) Oae, S. *Organic Chemistry of Sulfur*; Kagakudoujin: Kyoto, 1982. (c) Glass, R. S.; Petsom, A.; Hojjatie, M.; Coleman, B. R.; Duchek, J. R.; Klug, J.; Wilson, G. S. *J. Am. Chem. Soc.* **1988**, *110*, 4772−4778. (d) Tidwell, T. T. *Synthesis* **1990**, 857−870. (e) Pickersgill, I. F.; Marchington, A. P.; Rayner, C. *J. Chem. Soc., Chem. Commun.* **1994**, 2597−2598. (f) Vederas, J. C.; Liu, Y.-Q. *J. Org. Chem.* **1996**, *61*, 7856−7859. (g) Nakajima, N.; Ubukata, M. *Tetrahedron Lett.* **1997**, *38*, 2099−2102. (h) Majetich, G.; Hicks, R.; Reister, S. *J. Org. Chem.* **1997**, *62*, 4321−4326. (i) Kobayashi, K.; Obinata, T.; Furukawa, N. *Chem. Lett.* **1997**, 1175−1176.

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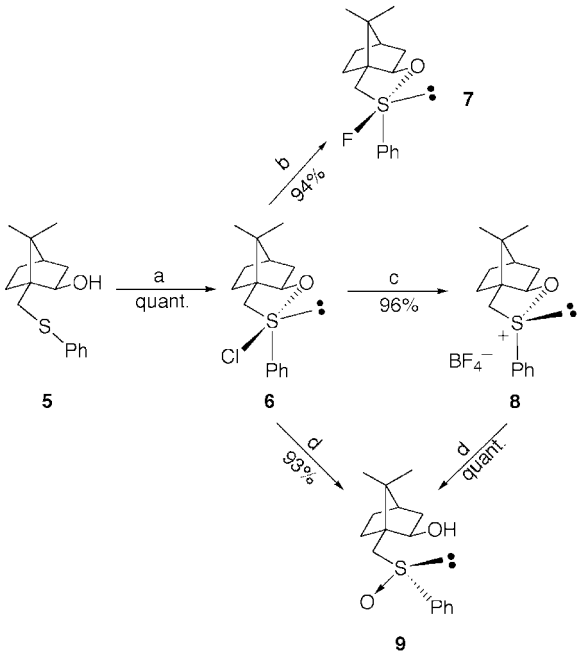
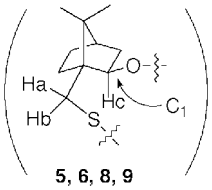
Scheme 3[a]



[a] Reagents and conditions: (a) *t*-BuOCl, CH_2Cl_2, 0 °C; (b) AgF, CH_2Cl_2, 0 °C; (c) $AgBF_4$, CH_2Cl_2, 0 °C; (d) satd $NaHCO_3$(aq).

Table 1. ^{1}H and ^{13}C NMR Chemical Shifts (ppm) of 5, 6, 8, and 9



5, 6, 8, 9

compd	Ha, Hb	Hc	C_1
5	2.96, 3.23	3.94	77.0
6	4.57, 4.69	4.34	100.4
8	4.21, 4.69	5.05	105.0
9	2.38, 3.35	4.20	77.2

at very low field compared to those of the corresponding sulfide **5** and sulfoxide **9** (Table 1). The chemical shift of the proton (H_c) in salt **8** appeared at ever lower field (5.05 ppm) as compared with that of the chlorophenylsulfurane **6** (4.34 ppm). In the ^{13}C NMR spectrum, the signal of C_1 appeared at 105.0 ppm while the signals of the corresponding carbon of sulfide **5** and sulfurane **6** appeared at 77.0 and 100.4 ppm, respectively. These results indicate that the sulfur atom is positively charged and the positive charge is delocalized onto the oxygen atom. The mass spectrum of **8** did not show a molecular peak except for $m/z = 261$ ($M^+ - BF_4$). These spectral features are consistent with the five-membered cyclic alkoxysulfonium salt **8**.

The structure of **8** was confirmed by a single-crystal X-ray crystallographic analysis (Figure 1). The X-ray data indicated that there is no covalent interaction between the anion and cation. The C−C and C−S bond lengths are within the expected values. The S−O bond

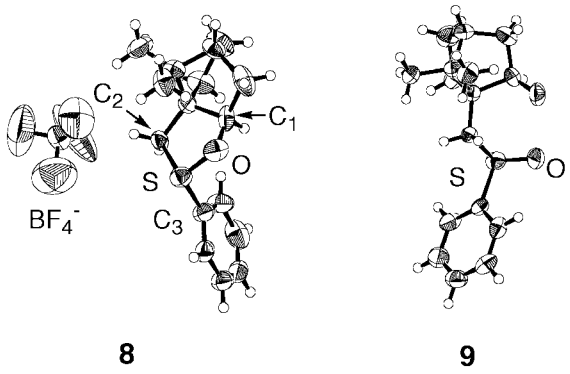


Figure 1. X-ray structures of **8** and **9**.

length of 1.598(8) Å is longer than the 1.49 ± 0.2 Å found for that in sulfoxides but significantly shorter than the S−O bond length of a spirosulfurane [1.686(6) Å].[6] This result could be interpreted in terms of the increased double-bond character of the S−O bond in **8**.[7] In addition, the C(3)−S−O, C(2)−S−O, and C(2)−S−C(3) bond angles of 107.2(5)°, 98.6(5)°, and 105.2(5)° in salt **8** are comparable to those found in the cyclic alkoxysulfonium salts reported by Glass et al.,[8] while the S−O−C(1) bond angle of 109.0(7)° of salt **8** is quite smaller than that of their six-membered salts [121.2(9)°]. Thus, the geometry about tetrahedral sulfur has a pyramidal geometric structure with *S* absolute configuration at the sulfur center as depicted in Figure 1.[9]

The hydrolysis of salt **8** was performed under the same condition employed for the hydrolysis of chlorosulfuranes. Stirring a solution of **8** in CH_2Cl_2 with saturated $NaHCO_3$-(aq)[10] at room temperature for 10 min gave sulfide **9** in quantitative yield as the sole product. The spectroscopic data of **9** are identical with that of the product obtained via the hydrolysis of chlorooxasulfurane, and the stereochemistry of the sulfoxide was unambiguously determined by an X-ray crystallographic analysis as shown in Figure 1, which indicated that the absolute configuration at the sulfur center is *R*.[9] Therefore, the reaction proceeded via the same stereochemical process as that of the chlorooxasulfurane.

Although the results we obtained do not exclude the possibility that the hydrolysis of chlorosulfuranes proceeds via an associative pathway, we now have supporting evidence that the reaction may proceed through a dissociative mechanism involving an alkoxysulfonium salt as an intermediate. We assume that an associative mechanism is operating in the presence of a strong nucleophile such as R^- (R = alkyl group), while a dissociative mechanism is operating in the presence of a weak nucleophile such as X^- (X = halogen) or H_2O.[11]

In summary, we have succeeded in the isolation of a chiral cyclic alkoxysulfonium salt which was prepared

(5) For recent examples on the isolation of optically active sulfonium salts, see: (a) Kimura, T.; Nakayama, H.; Furukawa, N. *Chem. Lett.* **1994**, 27−28. (b) Matsugi, M.; Hashimoto, K.; Inai, M.; Fukuda, N.; Furuta, T.; Minamikawa, J.; Otsuka, S. *Tetrahedron: Asymmetry* **1995**, *6*, 2991−3000.

(6) Zhang, J.; Saito, S.; Koizumi, T. *J. Am. Chem. Soc.* **1998**, *120*, 1631−1632.

(7) A referee has pointed out that this shortening may indicate a decrease in electronic repulsion between the two atoms.

(8) (a) Glass, R. S.; Setzer, W. N.; Prabhuu, D. G.; Wilson, G. S. *Tetrahedron Lett.* **1982**, *23*, 2335−2338. (b) Glass, R. S.; Hojjatie, M.; Setzer, W. N.; Wilson, G. S. *J. Org. Chem.* **1986**, *51*, 1815−1820. (c) Glass, R. S.; Petsom, A.; Wilson, G. S. *J. Org. Chem.* **1987**, *52*, 3537−3541.

(9) The assignment of the absolute configuration of the sulfur atom was based on the known absolute configuration of the borneol residue.

(10) This weak base was used to trap the acid formed by hydrolysis and shift the equilibrium. It is less possible that this weak base functions as a nucleophile.

from a chiral chlorooxasulfurane. Hydrolysis of the alkoxysulfonium salt afforded a sulfoxide with the same stereochemistry which was observed in the hydrolysis of a chlorooxasulfurane. This result is helpful on the understanding of the mechanism concerning the nucleophilic reactions of a pentacoordinated halooxachalcogenurane. Isolation and reaction of other chiral chalcogenonium salts are ongoing in our group.

Experimental Section

General. Common experimental procedures and instrumentation have been described previously.[1f] *J* values are given in hertz (Hz).

(1*S*)-10-(Phenylthio)-2-*exo*-borneol (5):[3] colorless oil; $[\alpha]^{24}_D$ −35.05 (*c* 2.44, $CHCl_3$); IR (neat) 3463, 2952, 1480, 1438, 1071, 1026, 737, 690 cm^{-1}; ^1H NMR δ 0.88 (s, 3H), 1.09 (s, 3H), 1.05−1.9 (m, 7H), 2.19 (br, 1H), 2.96 (d, J = 11.0, 1H), 3.23 (d, J = 11.0, 1H), 3.94 (dd, J = 3.9, 7.7, 1H), 7.15−7.4 (m, 5H); ^{13}C NMR δ 20.2, 21.0, 27.4, 31.3, 34.1, 39.5, 45.4, 48.2, 52.5, 77.0, 111.5, 126.1, 129.0, 129.1, 137.3; MS *m*/*z* 263 (M^+ + 1), 262 (M^+), 245, 153, 135, 123; HRMS calcd for $C_{16}H_{22}OS$ 262.1390, found 262.1353.

(1*S*,*R*$_S$)-5-Chloro-10,10-dimethyl-5-phenyl-5λ^4-thia-4-oxatricyclo[5.2.1.0^{3,7}]decane (6). To a solution of sulfide **5** (89 mg, 0.34 mmol) in anhydrous CH_2Cl_2 (4 mL) was added *t*-BuOCl dropwise at 0 °C under nitrogen atmosphere. The reaction mixture was stirred at 0 °C for 20 min; then evaporation of the solvent and excess reagents afforded chlorooxasulfurane **6** (101 mg) as a white solid in quantitative yield: ^1H NMR δ 0.99 (s, 3H), 1.17 (s, 3H), 0.8−2.35 (m, 7H), 4.34 (dd, J = 3.3, 7.7, 1H), 4.57 (d, J = 15.4, 1H), 4.69 (d, J = 14.8, 1H), 7.50−7.71 (m, 3H), 7.90−8.05 (m, 2H); ^{13}C NMR δ 20.0, 20.1, 26.4, 27.5, 37.1, 46.1, 47.2, 56.6, 56.9, 100.4, 123.8, 127.8, 129.4, 129.8, 132.7, 136.0; MS *m*/*z* 298 (M^+, ^{37}Cl), 296 (M^+, ^{35}Cl), 279, 277, 262, 260, 171, 253, 135, 126, 109, 93, 78, 67, 55; HRMS Calcd for $C_{16}H_{21}OSCl$ 298.0972 (M^+, ^{37}Cl), 296.1002 (M^+, ^{35}Cl), found: 298.0941, 296.1027.

(1*S*,*R*$_S$)-10,10-Dimethyl-5-fluoro-5-phenyl-5λ^4-thia-4-oxatricyclo[5.2.1.0^{3,7}] decane (7). To a solution of a chlorophenylsulfurane (prepared from 52.5 mg of sulfide, 0.20 mmol) in dry CH_2Cl_2 (4 mL) was added AgF (80 mg, 0.63 mmol) at 0 °C under a N_2 atmosphere. The whole mixture was stirred at 0 °C for 30 min, and the precipitates were filtered. The filtrate was evaporated to give the product in 94% yield (53 mg) as a white solid. This highly hygroscopic compound could not be fully characterized: ^1H NMR δ 0.96 (s, 3H), 1.13 (s, 3H), 1.2−1.38 (m, 2H), 1.61−1.91 (m, 3H), 1.95−2.01 (m, 1H), 2.08−2.29 (m, 2H), 4.32 (dd, J = 3.3, 7.7, 1H), 4.53 (d, J = 15.4, 1H), 4.63 (d, J = 15.4, 1H), 7.54−7.61 (m, 3H), 7.93−7.96 (m, 2H); ^{13}C NMR δ 20.0, 20.1, 26.5, 27.5, 37.2, 46.3, 47.4, 56.1, 57.3, 101.1, 128.1, 130.0, 131.5, 133.1.

Hydrolysis of Chlorosulfurane 6. To a solution of chlorooxasulfurane **6** (60 mg, 0.2 mmol) in CH_2Cl_2 (50 mL) was added saturated $NaHCO_3$ (ca. 2 mL) at room temperature in a separatory funnel. The two-phase solution was shaken vigorously and separated. The organic layer was washed with water (2 mL × 1) and brine (2 mL × 1) and dried over $MgSO_4$. Evaporation of solvent under reduced pressure gave the product (1*S*,*R*$_S$)-10-(phenylsulfinyl)-2-*exo*-borneol (**9**) as colorless crystals (52 mg) in 93% yield. The product was further purified by crystallization from hexane and CH_2Cl_2: mp 124−125 °C; $[\alpha]^{27}_D$ +133.0 (*c* 1.00, $CHCl_3$); IR (KBr) 3375, 2956, 1446, 1032, 995 cm^{-1}; ^1H NMR δ 0.80 (s, 3H), 1.06 (s, 3H), 1.2−2.0 (m, 7H), 2.38 (d, J = 13.2, 1H), 3.35 (d, J = 13.7, 1H), 4.14 (br d, J = 3.3, 1H), 4.20 (ddd, J = 1.9, 3.8, 5.8, 1H), 7.5−7.6 (m, 3H), 7.6−7.75 (m, 2H); ^{13}C NMR δ 20.1, 20.7, 27.4, 31.2, 38.7, 45.3, 48.5, 52.2, 60.0, 77.2, 123.9, 129.5, 131.3, 144.3; MS *m*/*z* 278 (M^+), 262, 260, 244, 229, 217, 201, 181, 153, 138, 135, 126, 110, 93, 78, 57. Anal. Calcd for $C_{16}H_{22}O_2S$: C, 69.02; H, 7.96. Found: C, 69.06; H, 7.92.

Recrystallization of the product from hexane and CH_2Cl_2 gave a crystal which was suitable for X-ray analysis. Crystallographic data for **9**: orthorhombic, space group $P2_12_12_1$ (No. 19) with a = 11.508(3) Å, b = 13.437(3) Å, c = 9.798(3) Å, V = 1515.1(6) Å^3, and Z = 4 (d_{calcd} = 1.220 g cm^{-3}); μ(Mo Kα) = 2.10 cm^{-1} absorption corrected by ω scans; 2013 total reflections, 1159 with $I > 3.00\sigma(I)$ were used in refinement; R = 4.2%, R_w = 4.2%. Further details of the crystal structure investigation are available on request from the Director of the Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge, CB2 1EZ (U.K.), on quoting the full journal citation.

Alkoxysulfonium Salt 8. To a solution of chlorooxasulfurane (101 mg, 0.34 mmol) in anhydrous CH_2Cl_2 (10 mL) was added silver tetrafluoroborate (66.3 mg, 0.34 mmol) at 0 °C under nitrogen atmosphere. The reaction mixture was stirred at 0 °C for 20 min, while the precipitate of AgCl deposited. Then filtration of AgCl and evaporation of the solvent gave optically pure alkoxysulfonium salt **8** as crystals (114 mg) in 96% yield. The product was further purified by crystallization from hexane and CH_2Cl_2. **8**: mp 150−151 °C; $[\alpha]^{26}_D$ +68.56 (*c* 1.08, $CHCl_3$); IR (KBr) 2953, 1443, 1395, 1084, 1034, 996, 752 cm^{-1}; ^1H NMR δ 0.90 (s, 3H), 1.13 (s, 3H), 1.31−1.39 (m, 1H), 1.63−1.69 (m, 1H), 1.82−1.99 (m, 2H), 2.02−2.11 (m, 1H), 2.15−2.30 (m, 1H), 2.38−2.44 (m, 1H), 4.21 (d, J = 14.3, 1H), 4.69 (d, J = 14.3, 1H), 5.05 (dd, J = 2.8, 7.7, 1H), 7.63−7.81 (m, 3H), 7.88−7.98 (m, 2H); ^{13}C NMR δ 19.7, 19.8, 26.3, 26.6, 37.4, 46.7, 47.4, 53.3, 59.8, 105.0, 128.9, 131.0, 131.1, 135.7; MS *m*/*z* 262, 261 ($M^+ - BF_4$), 260, 244, 229, 201, 153, 126, 110, 93, 79. Anal. Calcd for $C_{16}H_{21}BF_4OS$: C, 55.19; H, 6.08. Found: C, 55.05; H, 5.91.

Recrystallization of the product from hexane and CH_2Cl_2 gave a crystal which was suitable for X-ray analysis. Crystallographic data for **8**: orthorhombic, space group $P2_12_12_1$ (No. 19) with a = 13.653(3) Å, b = 15.915(4) Å, c = 7.544(2) Å, V = 1639.3(6) Å^3, and Z = 4 (d_{calcd} = 1.411 g cm^{-3}); μ(MoKα) = 2.38 cm^{-1} absorption corrected by ω scans; 1745 unique reflections, 1086 with $I > 3.00\sigma(I)$ were used in refinement; R = 8.2%, R_w = 8.0%. Further details of the crystal structure investigation are available on request from the Director of the Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge, CB2 1EZ (U.K.), on quoting the full journal citation.

Hydrolysis of Alkoxysulfonium Salt 8. To a solution of alkoxysulfonium salt **8** (19 mg, 0.055 mmol) in CH_2Cl_2 (30 mL) was added saturated $NaHCO_3$ (ca. 1 mL) at room temperature in a separatory funnel. The two-phase solution was shaken vigorously and separated. The organic layer was washed with water (2 mL × 1) and brine (2 mL × 1) and dried over $MgSO_4$. Evaporation of solvent under reduced pressure gave product **9** as crystals (16 mg) in quantitative yield.

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(11) (a) Kaplan, L. K.; Martin, J. C. *J. Am. Chem. Soc.* **1973**, *95*, 793−798. (b) Martin, J. C.; Perozzi, E. F. *J. Am. Chem. Soc.* **1974**, *96*, 3155−3168.