solution containing 0.1 M (2,4,5-trimethylphenyl)nitromethane (or 2,4,5-trimethylbenzyl nitrate), 0.5 M TNM, and 0.1 M 2,6-lutidine in acetonitrile (3 mL) did not lead to any decomposition of the starting material to 2,4,5-trimethylbenzaldehyde. However, 2,4,6-trimethylbenzyl nitrite slowly decomposed at room temperature to give 2,4,5-trimethylbenzaldehyde and reddish brown fumes (NO_2). Thus it is possible that 2,4,5-trimethylbenzaldehyde arose from the decomposition of initially formed 2,4,5-trimethylbenzyl nitrite.[81]

Quantum Yield for Side-Chain Nitration. The quantum yields were measured subsequent to the irradiation of the solution with an Osram 450-W high pressure xenon lamp that was focused through an aqueous IR filter, followed by an interference filter (10-nm bandpass, Edmund Scientific) as a monochromator. A Reinecke salt actinometer was used to calibrate the lamp intensity, as described by Wegner and Adamson.[82] In a typical experiment, 0.05 M arene and excess TNM in 2 mL of acetonitrile was placed in a 1-cm quartz precision cell and irradiated for a given period of time. For hexamethylbenzene and pentamethylbenzene, the quantum yields were measured at 505 nm, and for durene they were measured at 450 nm. The absorbance of the solutions at these wavelengths was always >1.5, and corrections were made for transmitted light. After photolysis, *p*-xylene was added as the internal standard and the side chain nitration products and the unreacted arene were quantitatively analyzed by gas chromatography. The quantum yield for formation of the side chain nitration products and that of the disappearance of the arene were an average of two runs in which the conversions were kept between 5-15%.

Acknowledgment. We thank the National Science Foundation and the Robert A. Welch Foundation for financial support. J. M.M. also gratefully acknowledges support from SOHIO, the Cleveland State College of Graduate Studies, and the donors of the Petroleum Research Fund, administered by the American Chemical Society. We thank M. A. J. Rodgers, S. J. Atherton, and the Center for Fast Kinetics Research [under support from the National Institute of Health (Grant No. RR 00886) and the University of Texas at Austin] for use of their laser facilities and the National Science Foundation for the funds to construct a laser-flash system in Houston. We also acknowledge the participation of T. Lund (U.H.) in the early stages of this study.

(81) Lachowicz, D. R.; Kreuz, K. L. *J. Org. Chem.* **1967**, *32*, 3885.
(82) Wegner, E. E.; Adamson, A. W. *J. Am. Chem. Soc.* **1966**, *88*, 394.

Intramolecular Dissociative Isomerization and the Presence of Trans Influence in 12-Sb-6 Ate Complexes and Their Protonolysis[1,2]

Yohsuke Yamamoto, Hisao Fujikawa, Hiroshi Fujishima, and Kin-ya Akiba*

Contribution from the Department of Chemistry, Faculty of Science, Hiroshima University, Higashisenda-machi, Hiroshima 730, Japan. *Received August 17, 1988*

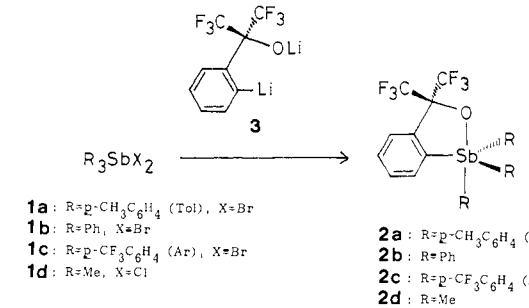
Abstract: The reaction of methyllithium with 3,3-bis(trifluoromethyl)-1,1,1-tris(*p*-methylphenyl)-3*H*-2,1-benzoxastilbole (10-Sb-5, **2a**) gave a 12-Sb-6 ate complex (**5a**). At −78 °C a single isomer (**5aA**) with the methyl group cis to the oxygen atom was formed. ^{19}F NMR of **5aA** showed a pair of quartets, indicating the presence of nonequivalent CF_3 groups. When the solution was warmed to room temperature, equilibration took place among three positional isomers, **5aA**, **5aB**, and **5aC**, and resulted in the ratio of 61:23:16 at 20 °C, respectively. The mechanism for the isomerization was concluded to be an intramolecular dissociation involving cleavage of an endocyclic Sb–O bond and pseudorotation of the resulting 10-Sb-5 intermediate. The mechanism was supported by kinetic measurements of the isomerization with or without HMPA (12-crown-4) and of quenching with **5a** with EtOH. Trans influence of the oxygen atom on the equilibrium ratio of the mixture of **5b**, which was generated by the reaction of *p*-$CF_3C_6H_4Li$ with **2a**, was observed. Ab initio calculation was carried out on model compounds H_5SbF^-, H_5SbOH^-, and $H_4SbF_2^-$ to support the electron-withdrawing effect of the electronegative atom on the trans hydrogen. Protonolysis of 12-Sb-6 (**5**) ate complexes was concluded to take place by the initial protonolysis at the oxygen atom to form zwitterion (**5**–H^+) which is followed by ring-opening to pentacoordinated antimony (**8**). A hydrocarbon is eliminated from **5**–H^+ during rapid equilibration between **5**–H^+ and **8**.

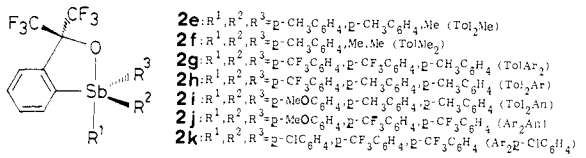
The synthesis, structure, and reaction of hypervalent compounds of main-group elements below the second row have been attracting increasing interest, and several successful reports for synthesizing those of the first row have recently expanded this area of chemistry.[3] Hypervalent compounds of the former class have shown characteristic features based on the essentially weak and polarizable nature of the hypervalent bond. Recently, Barton et al. reported extensive work on phenylation of enols, phenols, and amines by the use of 10-Bi-5 compounds.[4] We recently reported selective reductive coupling of two ligands, dehydrogenation of benzoins, and some other reactions using acyclic pentacoordinate antimony compounds and revealed rather unique characteristics of them.[5] Then we paid our attention to hexacoordinate antimony ate complexes, which were known to be unstable,[6] and only one

(1) For a preliminary account of a part of these results, see: Akiba, K-y.; Fujikawa, H.; Sunaguchi, Y.; Yamamoto, Y. *J. Am. Chem. Soc.* **1987**, *109*, 1245.
(2) The *N*-X-*L* designation was proposed previously: X, central atom; *N*, formal valence-shell electrons about an X; *L*, the number of ligands. See: Perkins, C. W.; Martin, J. C.; Arduengo, A. J.; Lau, W.; Algeria, A.; Kochi, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 7753.
(3) 10-C-5: Forbus, T. R.; Martin, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 5057. 10-B-5 and 12-B-6: Lee, D. Y.; Martin, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 5745. 10-F-2: Farnham, W. B. *Chem. Eng. News* **1986**, June 2, 22.
(4) Phenols and enols: Barton, D. H. R.; Finet, J.-P.; Khamsi, J.; Pichon, C. *Tetrahedron Lett.* **1986**, *27*, 3619, and references there cited. Amines: Barton, D. H. R.; Finet, J.-P.; Khamsi, J. *Tetrahedron Lett.* **1987**, *28*, 887, and references there cited.
(5) Akiba, K-y.; Shimizu, A.; Ohnari, H.; Ohkata, K. *Tetrahedron Lett.* **1985**, *26*, 3211. Akiba, K.-y.; Ohnari, H.; Ohkata, K. *Chem. Lett.* **1985**, 1577. Ohkata, K.; Ohnari, H.; Akiba, K-y. *J. Chem. Soc. Jpn.* **1987**, 1267. Akiba, K-y.; Okinaka, T.; Nakatani, M.; Yamamoto, Y. *Tetrahedron Lett.* **1987**, *28*, 3367. Yamamoto, Y.; Okinaka, T.; Nakatani, M.; Akiba, K-y. *J. Chem. Soc. Jpn.* **1987**, 1286.
(6) Hellwinkel, D. *Top. Curr. Chem.* **1983**, *109*, 1. *Gmelin Handbook of Inorganic Chemistry, 8th Ed; Sb Organoantimony Compounds*; Wieber, M., Ed.; Springer-Verlag: Berlin, 1985; Part 3, p 1.

0002-7863/89/1511-2276$01.50/0

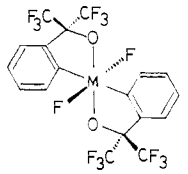
Scheme I





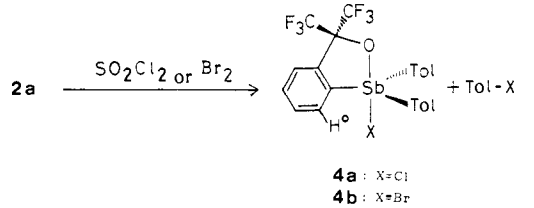
example of a covalent compound, i.e., $Ph_6Sb^-Li^+$, was characterized by Wittig,[7a] although several 12-Sb-6 compounds involving weak coordination have been reported tentatively as such.[7b] Some 12-Sb-6 species have been proposed as intermediates in the reactions of 10-Sb-5 with nucleophiles.[8]

As a preliminary communication we reported formation and isomerization of a 12-Sb-6 compound (**5a**) with a bidentate ligand (**3**), which was developed by Martin and was shown to be effective in stabilizing hypervalent molecules.[9] The mechanisms for isomerization of hexacoordinate compounds of typical elements have been studied in some cases recently.[10] Martin reported a nondissociative isomerization (Bailar twist; type c in Scheme VI) of a 12-Te-6 (**6**)[10c] and a dissociative isomerization involving an

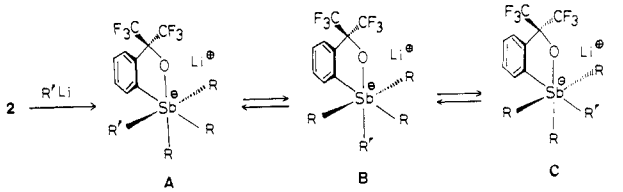


exocyclic S–F bond cleavage (type a in Scheme VI) of the corresponding 12-S-6 (**7**).[10d] The results indicated that the size of the central element played an important role in the isomerization. It is interesting to clarify the mechanism for the isomerization of the anionic 12-Sb-6 (**5**); the central element of antimony has a similar size to the tellurium. Here we report evidence for an intramolecular dissociative isomerization (type b in Scheme VI) of a kinetically formed compound **5aA** to one of the other isomers **5aB**.

Scheme II



Scheme III



	R	R'
5a	p-$CH_3C_6H_4$ (Tol)	Me
5b	p-$CH_3C_6H_4$ (Tol)	p-$CF_3C_6H_4$ (Ar)
5c	p-$CH_3C_6H_4$ (Tol)	p-$MeOC_6H_4$ (An)
5d	p-$CF_3C_6H_4$ (Ar)	p-$CH_3C_6H_4$ (Tol)
5e	p-$CF_3C_6H_4$ (Ar)	p-$MeOC_6H_4$ (An)
5f	p-$CF_3C_6H_4$ (Ar)	Ph
5g	p-$CF_3C_6H_4$ (Ar)	p-ClC_6H_4
5h	p-$CF_3C_6H_4$ (Ar)	p-$CF_3C_6H_4$ (Ar)

Trans influence of ligands in hexacoordinate complexes containing a main-group element as a central atom has scarcely been studied compared to that of transition-metal complexes.[11] Main subjects that have been discussed include lengthening and weakening (or shortening, strengthening) of the bond between a central atom and a ligand. We here report trans influence of the oxygen atom on the equilibrium ratio of 12-Sb-6 ate complexes. The result indicates that the oxygen atom causes relative electron deficiency to the trans ligand. The discussion is supported by ab initio calculation of model compounds such as H_5SbF^-, H_5SbOH^-, and $H_4SbF_2^-$.

Reactions of 10-Sb-5 (**2**) with electrophiles and protonolysis of 12-Sb-6 (**5**) are also described.

Preparation of Stiboranes 2. 1,1,1-Trisubstituted 3,3-bis(trifluoromethyl)-3*H*-2,1-benzoxastiboles **2** were prepared by the method outlined in Scheme I. The reaction of triarylantimony dibromides (or trimethylantimony dichloride) (**1a–1d**, R_3SbX_2) with the dilithiated reagent **3**[12] of bis(trifluoromethyl)benzyl alcohol gave **2** in fair to good yields. Compounds **2** are stable to heat (<250 °C) and to atmospheric moisture. They could be purified by flash column chromatography (SiO_2) to give colorless crystals. Related compounds bearing different substituents on the antimony were also isolated from the quenching experiment of ate complexes (**5**) by protic acids (vide infra).

Reaction of 2 with Electrophiles. Compounds **2** were inert toward various electrophiles. For example, **2a** did not react with EtCOCl, $CH_2{=}N^+Me_2I^-$, and $(NH_4)_2Ce(NO_3)_6$ at 60–70 °C for over 10 h. But it gave a stiborane (**4a**, **4b**) with an Sb–halogen bond in 80–90% yield by treatment with sulfuryl chloride or bromine (Scheme II). Compounds **4a** and **4b** were also quite stable and interesting in relation to the recent concern for the (covalent or ionic) nature of the hypervalent element–halogen bond.[13] The Sb–halogen bond of **4** may be covalent based on the high solubility to benzene and chloroform and also the high stability to ethanol. The low-field chemical shift of the proton (H°) [**4a**: δ 8.68 (dd, J = 6.6, 2.4 Hz). **4b**: δ 8.73 (dd, J = 6.8, 2.4 Hz in $CDCl_3$)] also shows the presence of a hypervalent antimony–halogen bond.[13a]

Synthesis, Characterization, and Isomerization of 12-Sb-6 (5a). The reaction of 1 equiv of methyllithium with **2a** gave a hexacoordinate antimony ate complex (**5a**) (Scheme III). At low

(7) (a) Wittig, G.; Clauss, K. *Justus Liebigs Ann. Chem.* **1952**, *577*, 26. (b) DiBianca, F.; Rivarola, E.; Spek, A. L.; Meinema, H. A.; Noltes, J. G. *J. Organomet. Chem.* **1973**, *63*, 293. Ferguson, G.; Hawley, D. M. *Acta Crystallogr., Sect. B* **1974**, *30*, 103. Schwarz, W.; Guder, H. J.; *Acta Crystallogr., Sect. A* **1978**, *34*, S123. Schmidbaur, H.; Milewski-Mahrla, B.; Wagner, F. E. *Z. Naturforsch., Part B* **1983**, *38*, 1477. Holmes, R. R.; Day, R. O.; Chandrasekhar, V.; Holmes, J. M. *Inorg. Chem.* **1987**, *26*, 157.

(8) Daniel, H.; Paetsch, J. *Chem. Ber.* **1968**, *101*, 1451. Doleshall, G.; Nesmeyanov, N. A.; Reutov, O. A. *J. Organomet. Chem.* **1971**, *30*, 369. Nesmeyanov, N. A.; Borisov, A. E.; Novikova, N. N.; Fedin, E. I.; Petrovski, P. V. *Bull. Acad. Sci. USSR. Div. Chem. Sci. (Engl. Transl.)* **1973**, 1776. McEwen, W. E.; Briles, G. H.; Giddings, B. E. *J. Am. Chem. Soc.* **1969**, *91*, 7079. McEwen, W. E.; Lin, C. T. *Phosphorus Relat. Group V Elem.* **1974**, *3*, 229.

(9) Martin, J. C. *Science (Washington, D.C.)* **1983**, *221*, 509. Martin, J. C.; Perozzi, E. F. *Science (Washington, D.C.)* **1976**, *191*, 154. Hayes, R. A.; Martin, J. C. In *Organic Sulfur Chemistry: Theoretical and Experimental Advances*; Csizmadia, I. G., Mangini, A., Bernardi, F., Eds.; Elsevier: Amsterdam, 1985; Chapter 8, p 408.

(10) (a) Font Freide, J. J. H. M.; Tripett, S. *J. Chem. Soc., Chem. Commun.* **1980**, 157; (b) *Ibid.* **1980**, 934. (c) Michalak, R. S.; Wilson, S. R.; Martin, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 7529. (d) Michalak, R. S.; Martin, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 1683.

(11) Shustrovich, E. M.; Buslaev, Y. A. *Inorg. Chem.* **1976**, *15*, 1142, and references there cited.

(12) Perrozzi, 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*, 7049.

(13) (a) Granoth, I.; Martin, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 2711. (b) Livant, P. D. *J. Org. Chem.* **1986**, *51*, 5384. (c) Akiba, K-y.; Ohdoi, K.; Yamamoto, Y. *Tetrahedron Lett.* **1988**, *29*, 3817.

Table I. Time Dependence of the Isomer Ratio of **5b** Prepared from **2a** and p-$CF_3C_6H_4Li$[a]

compd	time				
	10 min	3 h	17 h	36 h	66 h
5bA	98	94	90	83	74
5bB	1	1	2	5	6
5bC	1	5	8	12	20

[a] At 25 °C.

Table II. Time Dependence of the Isomer Ratio of **5b** Prepared from **2h** and p-$CH_3C_6H_4Li$[a]

compd	time				
	0 min	5 min	40 min	8 h	32 h
5bA	17	13	24	31	51
5bB	70	60	39	24	11
5bC	13	27	37	45	38

[a] At 25 °C.

temperatures the exclusive formation of a single isomer (**5aA**) was clearly demonstrated by ^{19}F NMR, which showed the presence of only a pair of quartets [δ −74.2 and −74.8 ($^4J_{F\text{-}F}$ = 9 Hz at −50 °C)][14] of nonequivalent CF_3 groups at −78 °C. When the solution was warmed to −20 °C, a new singlet **5aB** appeared to give an equilibrium mixture within 1.5 h; the ratio of **5aA** to **5aB** was 3.8:1 at that temperature. At ~0 °C, another singlet **5aC** appeared.[15] At 20 °C equilibrium among three isomers, **5aA**, **5aB**, and **5aC**, was attained within 10 min as 61:23:16.[16] The exclusive kinetic selectivity observed for the formation of **5aA** from **2a** can be ascribed to the complexation of methyllithium with the oxygen atom of **2a** and also to the least steric hindrance during the approach of the nucleophile to **2a**. We cannot determine the structure of **5aB** and **5aC** exactly at this stage; we assume that the ate complex **5a** with the methyl group trans to the oxygen atom (**5aB**) is preferable to that with the p-tolyl group trans (**5aC**) based on the trans influence of the oxygen atom.[17] The same equilibrium was established by the reaction of **2e** with p-tolyllithium. The reaction was carried out at −78 °C, and ^{19}F NMR of the mixture was measured at −50 °C to show **5aA**:**5aB**:**5aC** = 84:10:6.[18]

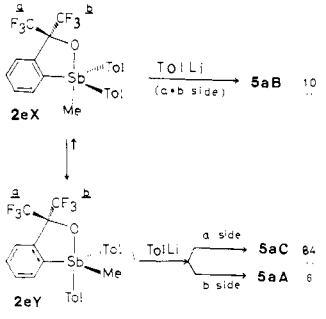
(14) The chemical shift fluctuated slightly according to the concentration of the solution and the temperature measured. The data in the text was measured in ca. 0.01–0.02 mol·L^{-1}. The list of chemical shifts of **5a** and **2** at −50 and 25 °C was cited in footnote 16.

(15) We illustrated the octahedral structure of **5** because the number of isomers detected (three in this case) was consistent with the structure. The number of isomers should be six (all isomers have nonequivalent CF_3 groups) in trigonal prism structure and nine (four isomers have nonequivalent CF_3 and the other five have equivalent ones) in bicapped tetrahedral structure.

(16) It should be noted that the two isomers **5aB** and **5aC**, which showed a singlet in ^{19}F NMR, could be differentiated from the starting **2a**. The ^{19}F NMR chemical shifts (δ, ppm) of **5a** and **2**: **5aA**, −74.2 and −74.8; **5aB**, −73.2; **5aC**, −73.9; **2a**, −75.1; **2b**, −75.5 (at −50 °C); **5aA**, −74.0 and −74.3; **5aB**, −74.0; **5aC**, −73.8; **2a**, −75.0; **2b**, −75.1 (at 25 °C). When the reaction was carried out with less than 1 equiv of methyllithium, we could observe the signals of the three isomers of **5a** and starting **2a**, separately.

(17) The assignment for **5aB** and **5aC** was changed from that in the preliminary communication.[1]

(18) The equilibrium ratio between **2eY** and **2eX** can be calculated as (84



+ 6):10, but the difference of reactivity in **2eY** for path a and path b (84:6) cannot be explained at present.

Scheme IV

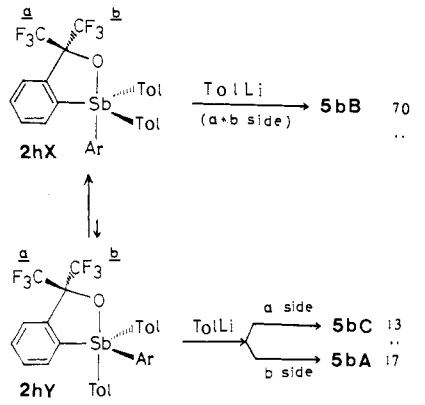
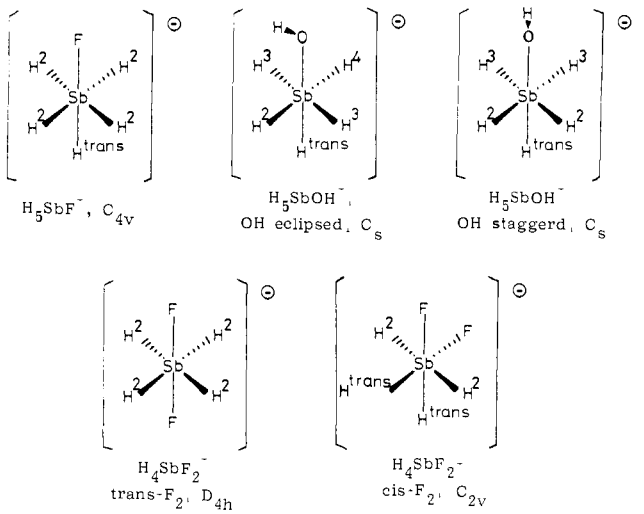


Chart I



When the mixture was warmed to 20 °C, the equilibrium ratio of the three isomers became the same as that in the reaction of **2a** with methyllithium within 10 min.

In order to examine the electronic effect of substituents to the equilibrium, the reaction of p-$CF_3C_6H_4Li$ with **2a** was tried to afford **5bA** almost exclusively at −78 °C (Table I). Although 85-MHz ^{19}F NMR of the solution appeared as a singlet and could not discriminate the nonequivalent CF_3 groups on the bidentate ligand, high-field ^{19}F NMR (470 MHz) showed the presence of a pair of quartets cleanly. The rate of isomerization of **5bA** was very much slower than that of **5aA**. Even when the solution of **5bA** was warmed to 25 °C, signals due to the other isomers, **5bB** and **5bC**, appeared only gradually. The isomerization could be followed by $CF_3C_6H_4$ signals of 85-MHz ^{19}F NMR at room temperature. After 66 h the ratio of **5bA**:**5bB**:**5bC** became 74:6:20. At this stage the assignment of **5bB** and **5bC**, both of which showed a singlet for CF_3 (bidentate ligand) groups, was not clear, but the chemical shift of each isomer in ^{19}F NMR was assigned tentatively (vide infra) [$CF_3C_6H_4$: **5bA**, **5bB**, **5bC**; δ −62.1, −62.6, −62.2 (at −50 °C), −62.2, −62.6, −62.1 (at 35 °C). CF_3 (bidentate ligand): **5bA**, **5bB**, **5bC**; δ −73.75 and −73.85 (q), −73.70 (s), −73.65 (s)]. The relatively high field $CF_3C_6H_4$ signal (δ −62.6) assigned to **5bB** was characteristic (vide infra). In order to determine the effect of the substituent on the equilibrium ratio, **5b** was generated via a different path, i.e., the reaction of **2h** with p-$CH_3C_6H_4Li$ was carried out at −78 °C. One of $CF_3C_6H_4$ singlets (δ −62.6) was predominantly observed by ^{19}F NMR of the solution at −50 °C. The kinetic ratio was 17:70:13 (**5bA**:**5bB**:**5bC**) and the ratio became 51:11:38 after 32 h (Table II).

The kinetic preference for the isomer **5bB** gave a basis for the assignment of the structure, because electronegative groups are known to prefer the apical position in the trigonal-bipyramidal pentavalent structure (apicophilicity).[19] In **2h**, therefore, the

Table III. Total Energies, Charge Densities, and Bond Lengths for H_5SbF^-, H_5SbOH^- (OH eclipsed and staggered), and $H_4SbF_2^-$ (with fluorines cis and trans)[a]

	compd				
	H_5SbF^-	H_5SbOH^- (OH eclipsed)	H_5SbOH^- (OH staggered)	$H_4SbF_2^-$ (trans)	$H_4SbF_2^-$ (cis)
bond length, Å					
d(Sb-H^{trans})	1.770	1.778	1.777		1.757
d(Sb-H^2)	1.766	1.791	1.785	1.751	1.735
d(Sb-H^3)		1.773	1.762		
d(Sb-H^4)		1.756			
d(Sb-X)	1.923	1.996	1.997	1.918	1.906
	(X:F)	(X:OH)	(X:OH)	(X:F)	(X:F)
charge density					
q(Sb)	+0.903	+0.901	+0.900	+1.229	+1.113
q(H^{trans})	-0.242	-0.246	-0.246		-0.244
q(H^2)	-0.276	-0.308	-0.299	-0.277	-0.259
q(H^3)		-0.286	-0.269		
q(H^4)		-0.257			
q(X)	-0.558	-0.828	-0.829	-0.561	-0.554
	(X:F)	(X:OH)	(X:OH)	(X:F)	(X:F)
total energy -E, kcal/mol	67110.1	52102.0	52101.8	128864.2	128869.4
fixed symmetry	C_{4v}	C_s	C_s	D_{4h}	C_{2v}

[a] The Sb-H bond trans to the electronegative F is calculated to be generally longer than the Sb-H bond cis to F by this method.

oxygen atom and the p-$CF_3C_6H_4$ group are expected to be mainly in the apical position in spite of very rapid equilibration (**2hX** ⇄ **2hY**) by Berry pseudorotation (Scheme IV). Attack by a lithium reagent should take place from an equatorial edge between the bidentate and a monodentate ligand due to complexation of the lithium cation with lone-pair electrons of the oxygen atom. Thus, **5bB** is formed by the reaction of the major isomer **2hX** with p-$CH_3C_6H_4Li$ from both the *a* and *b* sides (70%). On the other hand, **5bA** and **5bC** are afforded by the reaction of the minor isomer **2hY** with p-$CH_3C_6H_4Li$ from the *b* side and *a* side in a comparable ratio (17%:13%), respectively. An equilibrium ratio between **2hX** and **2hY** can be easily obtained as 70:30 at -78 °C from the above result. According to the rationalization, equilibrium between **2eX** (apical Me) and **2eY** (apical tolyl) can be calculated as 10:90 at -78 °C,[18] and this is also consistent with the apicophilicity of the substituents.

From these results, it can be concluded that thermodynamic stability falls in the order of **5bA** > **5bC** > **5bB**, (ca. 6:3:1); hence the isomer (**5bB**) that bears the more electronegative group anti to the oxygen atom is the least stable and the stabilities of **5bA** and **5bC** are almost equal on the basis of statistics. There may be a steric feature to determine the thermodynamic stability of **5a**.

Ab Initio Calculation on Model Compounds H_5SbF^-, H_5SbOH^-, and $H_4SbF_2^-$. GAUSSIAN 80 was used in the calculation on 12-Sb-6 compounds. Effective core potential presented by Wadt and Hay[20] was used for the core electrons of Sb, and 3-21G basis sets with d orbitals were used for the valence electrons of Sb. The other atoms, H, F, and O, were described by 3-21G basis sets. To test the validity of the calculation, the optimum bond length of SbF_6^- was calculated to be 1.842 Å and was in close agreement with the bond lengths obtained by X-ray diffraction of $K^+SbF_6^-$ (1.841-1.849 Å)[21] and $Li^+SbF_6^-$ (1.877 Å).[22] All molecular geometries were optimized within fixed symmetry (Chart I). Total energies, bond lengths, and charge densities for H_5SbF^-, H_5SbOH^- (OH eclipsed and OH staggered), and $H_4SbF_2^-$ (cis and trans) are listed in Table III.

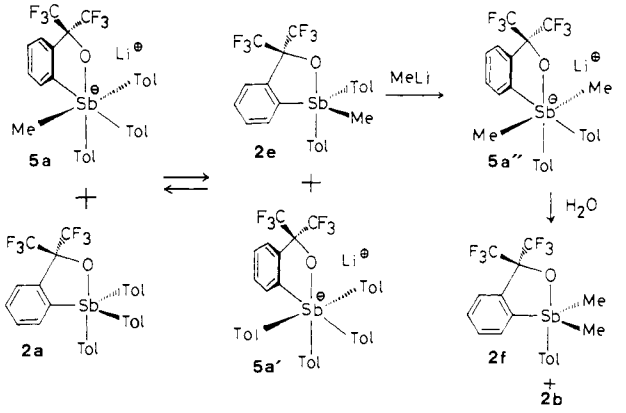
From the results the following observations can be made: (i) the charge density of hydrogen(s) trans to the electronegative atom is(are) always less than that of the cis hydrogen, (ii) the cis isomer of $H_4SbF_2^-$ is considerably more stable than the trans one (5.2 kcal/mol), and (iii) the orientation of the oxygen lone pair does not affect the energy and charge density significantly. In view of the results, the thermodynamically least stable isomer of **5b** should be **5bB** since the electronegative p-$CF_3C_6H_4$ group lies in the trans position to the electronegative oxygen atom. The above prediction is consistent with the assignment for **5bB**.

Table IV. ^{19}F NMR Chemical Shifts for the $CF_3C_6H_4$ (Ar) Group in **5eA**, **5dA**, **5fA** and **5h** Prepared from **2c** and p-XC_6H_4Li[a]

compd (R')			
5eA (p-$MeOC_6H_4$)	**5dA** (p-$CH_3C_6H_4$)	**5fA** (Ph)	**5h** (p-$CF_3C_6H_4$)
-62.59	-62.63	-62.63	-62.77
-62.69	-62.72	-62.71	-62.81
-63.03	-63.04	-63.06	-63.17

[a] At 35 °C.

Scheme V



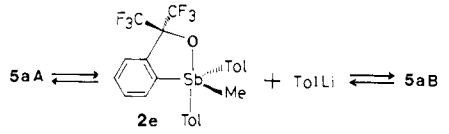
It is interesting to note that the $CF_3C_6H_4$ group of **5bB** showed the ^{19}F signal (δ -62.6) at the highest field among these isomers. The ^{19}F chemical shift of a $CF_3C_6H_4$ group was reported to shift to higher field according to increased electron-withdrawing effect of the para substituent.[23] The trend was confirmed in this system by the addition of para-substituted phenyllithium (p-XC_6H_4Li) into **2c** [$RfSbAr_3$: (Rf, bidentate ligand; Ar, p-$CF_3C_6H_4$)]. In each case, ate complexes **5dA**, **5eA**, **5fA**, and **5h** [$RfSbAr_3(p$-$XC_6H_4)]^-Li^+$ were generated in situ. The chemical shifts of all the three singlets for the $CF_3C_6H_4$ group of **5eA**, **5dA**, **5fA**, and **5h** were shifted to higher field gradually by the introduction of the more electronegative group (p-XC_6H_4) (Table IV). Hence, the apical oxygen atom is confirmed to be electron-withdrawing.

Mechanism of Isomerization of 12-Sb-6 (5a). In order to scrutinize the mechanism of isomerization of **5**, we tried to set up exact reaction conditions and found that intermolecular ligand transfer took place as a side reaction when solutions of more than 0.03 M were used or the reaction was run in an NMR tube. When

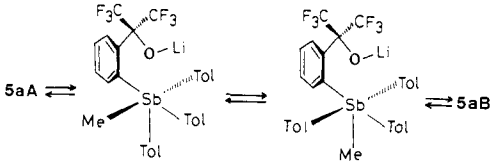
(19) Muetterties, E. L. *Acc. Chem. Res.* **1970**, *3*, 266.
(20) Wadt, W. R.; Hay, P. J. *J. Chem. Phys.* **1985**, *82*, 284.
(21) Kruger, G. J.; Pistorius, C. W. F. T.; Heyns, A. M. *Acta Crystallogr.* **1976**, *B32*, 2916.
(22) Burns, J. H. *Acta Crystallogr.* **1962**, *15*, 1098.
(23) Brownlee, R. T. C.; Craik, D. J. *Aust. J. Chem.* **1980**, *33*, 2555.

Scheme VI

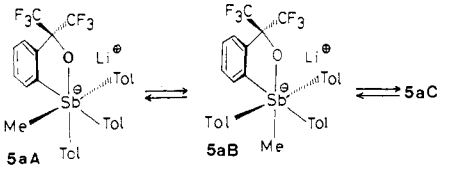
(a) an intermolecular Sb-C dissociative mechanism



(b) an intramolecular Sb-O dissociative mechanism



(c) an intramolecular nondissociative mechanism (Bailar twist etc)



the reaction of **2a** with methyllithium was carried out *in an NMR tube* and was quenched with protic acids (or solvents), ca. 10% of **2f** ($TolMe_2$) was obtained in addition to **2a** and **2e**. We were surprised by the result because only **2a** and **2e** were isolated in almost quantitative yield when the reaction of **2a** with methyllithium was carried out *in a flask* with stirring. We assumed the discrepancy might be caused by the local heterogeneity of the solution in an NMR tube and that intermolecular ligand transfer between **2a** and **5a** took place to form other 12-Sb-6 species such as **5a′** and **5a″**; the latter gave **2f** by quenching with water (Scheme V). The assumption was supported by the fact that **2f** was formed slowly when **2a** or **2e** was present in the solution of **5a**.[24] Therefore, the kinetic results described in this paper were obtained from the following procedures. Thus, the reaction of **2a** with methyllithium was carried out in a flask with stirring at −78 °C, and the resulting solution (0.01–0.02 M) was transferred under nitrogen to an NMR tube at that temperature by using a double-ended needle. Then the resulting solution was quenched with protic acids in an NMR tube after rate measurement; only **2a** and **2e** were obtained, which was consistent with the result obtained by a direct quenching experiment of a solution prepared in a flask.

The isomerization between **5aA** and **5aB** at −20 °C could be followed by ^{19}F NMR, and the rate was calculated[25] to be $(1.9 \pm 0.1) \times 10^{-4}$ s^{-1}, which was independent of the equivalent of added methyllithium (more or less than 1 equiv). The observation ruled out an associative isomerization mechanism involving attack of methyllithium at antimony in **5a** to form a heptacoordinate intermediate as well as an intermolecular equilibrium between penta- (**2a**) and hexacoordinate (**5a**) antimony. Then the following three mechanisms for the isomerization depicted in Scheme VI are possible: (a) an intermolecular Sb–C dissociative mechanism, (b) an intramolecular Sb–O dissociative mechanism, and (c) a nondissociative mechanism such as the Bailar twist. The rate of quenching of the mixture of **5aA** and **5aB** was measured at −20 °C with 10–100 equiv of EtOH (total concentration of EtOH, 0.6–1.4 M) to be $(1.8 \pm 0.1) \times 10^{-5}$ $L \cdot mol^{-1} \cdot s^{-1}$. Thus, the rate with 1 M EtOH was ca. 10 times slower than that of the equilibration at −20 °C. The result provided strong evidence against the intermolecular dissociative mechanism (a) involving a monodentate exocyclic Sb–C cleavage because the resulting free *p*-tolyllithium or methyllithium should react immediately with the large excess of EtOH instead of less than 1 equiv of the pentavalent antimony. But there could still be a possibility that *p*-tolyllithium reacted faster with **2e** than with EtOH.[26] Therefore, 2 equiv of *p*-tolyllithium was used to react with **2e** in the presence of 33 equiv of EtOH at −20 °C. But **5a** was not detected at all and only **2e** was observed by ^{19}F NMR. The result indicated that the lithium reagent reacted very much faster with the large excess of EtOH than with the small amount of **2e** present under the reaction conditions.

The rate of the isomerization was clearly decelerated by the addition of hexamethylphosphoric triamide (HMPA) or 12-crown-4. After 10 equiv of HMPA or 12-crown-4 was added to the solution of **5aA** at −50 °C, the mixture was warmed to −20 °C. The isomerization of **5aA** did not take place in the presence of HMPA and proceeded very slowly (**5aA**:**5aB** = 97:3 after 1.5 h) in the presence of 12-crown-4 at that temperature. The ratio changed to 78:12:9 (**5aA**:**5aB**:**5aC**) after 15 min at 25 °C. The slowed rate of the equilibration by the addition of 12-crown-4 was confirmed by the fact that the ratio described above did not change at −20 °C for 1 h. Thus, the former ratio (**5aA**:**5aB** = 97:3) and the above one were found not to be an equilibrium ratio at −20 °C. Even at 20 °C only gradual increase of **5aB** was observed with HMPA. At 25 °C it took 2–3 days with HMPA to attain the equilibrium (**5aA**:**5aB**:**5aC** = 69:24:7). The result indicated that the lithium cation played a key role in the isomerization and provided evidence for the dissociative mechanism (b) involving an endocyclic Sb–O cleavage, because any role of a lithium cation is not involved in the Bailar twist mechanism (c). It is interesting to note that the addition of *N,N,N′,N′*-tetramethylethylenediamine (TMEDA) affected only slightly the rate of isomerization, which was measured to be 1.2×10^{-4} s^{-1} at −20 °C. The value was slightly less than that without additives. The observation was consistent with recent reports that the solvating ability of nitrogen donors toward Na^+ and Li^+ was not as strong as was expected

Scheme VII

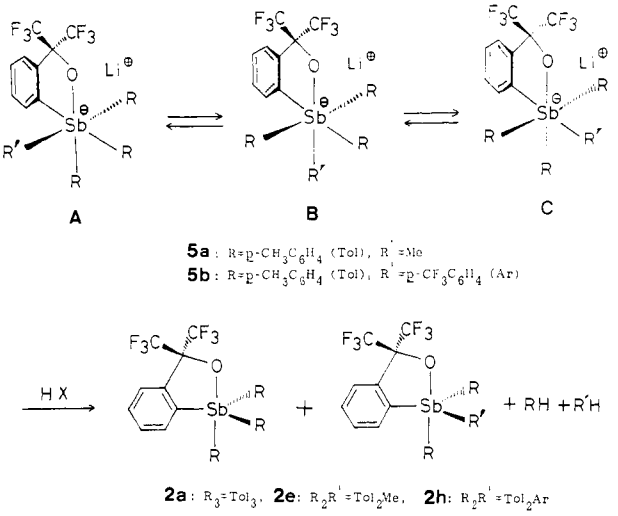


Table V. Quenching of the Equilibrium Mixture of **5a** with Several Protic Acids[a]

protic acid	pK_a	ratio of **2e**:**2a**
EtOH	17.0	94.0:6.0
H_2O	15.7	93.7:6.3
$2,6\text{-}Me_2C_6H_3OH$	10.6	96.0:4.0
PhOH	10.0	98.4:1.6
CH_3CO_2H	4.8	99.3:0.7

[a] Total isolated yield of **2a** and **2e** was 90–95%.

(24) When **2a** or **2e** remained in the solution of **5a**, a gradual increase of **2f** was observed at room temperature. But the rate was not so fast (a few percent per day), the rate of isomerization at −20 °C described in the text, therefore, was not affected by the intermolecular reaction between **2** and **5**. Experimental results adopted in this paper were obtained by ideal procedures described in the text.

(25) At −20 °C, no detectable amount of **5aC** was observed after the equilibration between **5aA** and **5aB** was completed. The rate of the equilibration, therefore, could be calculated by the reversible first-order kinetics.

(26) We thank Professor H. J. Reich (University of Wisconsin, Madison) for the suggestion of the possibility and the experimental conditions to check it.

from the Gutmann donor number scale.[27]

Protonolysis of 5. Protic acids (or solvents) reacted with a mixture of ate complexes (**5**) to effect quantitative cleavage of the exocyclic Sb–C bond and afforded a mixture of **2**. The cleavage of the endocyclic Sb–C bond was not observed at all. When an equilibrium mixture of **5a** was quenched at room temperature, **2e** was isolated as a major product and **2a** as a minor product in every case. For example, the ratio of **2e**:**2a** was 94:6 and the combined yield was 95% when a mixture of **5a** was quenched with water. When an equilibrium mixture of **5a** was quenched with various protic acids, the ratios of **2e**:**2a** were affected slightly, but definitely, by the pK_a of the acids (Table V). The results show that the stronger the quenching acids are the higher the ratio of **2e**:**2a**, and even the effect of steric hindrance is noticeable by comparison of the ratios obtained from 2,6-dimethylphenol and unsubstituted phenol. These facts clearly show that the Sb–C(tolyl) bond is much more reactive to protic acids than the Sb–C(methyl) bond. This is consistent with the reactivity of 10-Si-5 siliconates.[28]

In order to elucidate the electronic effect on the protonolysis of an ate complex, **5b** was prepared in situ by the reaction of **2h** wtih *p*-$CH_3C_6H_4Li$ at 0 °C. An aliquot of the solution was taken out at appropriate time intervals and the ratio of the three ate complexes (**5bA**:**5bB**:**5bC**) was measured by ^{19}F NMR, then the solution was quenched with 100 equiv of acetic acid, and the resulting **2a** and **2h** were determined quantitatively. The results are shown in Table VI. These were analyzed by the least-squares method to give the product ratio of **2h** (Tol–Sb bond cleavage):**2a** (Ar–Sb bond cleavage) for each ate complex, thus for **5bA**, (68 ± 15):(32 ± 15), for **5bB**, (71 ± 8):(29 ± 8), and for **5bC** (52 ± 17):(48 ± 17). Hence, reactivity ratios of Tol–Sb bond:Ar–Sb bond become for **5bA**, 1.0:1.4, for **5bB**, 1.0:1.2, and for **5bC**, 1.0:2.8. The Ar–Sb bond is apparently more reactive to acetic acid than the Tol–Sb bond in each ate complex. These included, however, considerably large statistical errors in spite of careful experimentation. We were forced to conclude here that the trans effect of the reactivity of **5b** was not so clearly observed as compared to the trans influence on the thermodynamic stability. Therefore, we pursued the protonolysis of almost pure **5bA** generated from **2a** and ArLi (*p*-$CF_3C_6H_4Li$) with several kinds of acids such as water, phenol, acetic acid, monochloro- and dichloroacetic acid, and trifluoroacetic acid. The ratio of **2h** to **2a** obtained was constant for every protic acid used (**2h**:**2a** = 59:41). Then almost pure **5A**-type complexes were generated by the following combination and quenched with 100 equiv of acetic acid or a large excess of water, and the yield of the resulting two compounds were determined quantitatively:

$$\mathrm{Tol_3}\ (\mathbf{2a}) + p\text{-}\mathrm{CF_3C_6H_4Li} \rightarrow \mathbf{5bA} \xrightarrow{\mathrm{H^+}} \mathrm{Tol_3}\ (\mathbf{2a}, 41\%) + \mathrm{Tol_2Ar}\ (\mathbf{2h}, 59\%) \quad (1)$$

$$\mathrm{Tol_3}\ (\mathbf{2a}) + p\text{-}\mathrm{MeOC_6H_4Li} \rightarrow \mathbf{5cA} \xrightarrow{\mathrm{H^+}} \mathrm{Tol_3}\ (\mathbf{2a}, 62\%) + \mathrm{Tol_2An}\ (\mathbf{2i}, 38\%) \quad (2)$$

$$\mathrm{Ar_3}\ (\mathbf{2c}) + p\text{-}\mathrm{CH_3C_6H_4Li} \rightarrow \mathbf{5dA} \xrightarrow{\mathrm{H^+}} \mathrm{Ar_3}\ (\mathbf{2c}, 15\%) + \mathrm{Ar_2Tol}\ (\mathbf{2g}, 85\%) \quad (3)$$

$$\mathrm{Ar_3}\ (\mathbf{2c}) + p\text{-}\mathrm{MeOC_6H_4Li} \rightarrow \mathbf{5eA} \xrightarrow{\mathrm{H^+}} \mathrm{Ar_3}\ (\mathbf{2c}, 48\%) + \mathrm{Ar_2An}\ (\mathbf{2j}, 52\%) \quad (4)$$

$$\mathrm{Ar_3}\ (\mathbf{2c}) + p\text{-}\mathrm{ClC_6H_4Li} \rightarrow \mathbf{5gA} \xrightarrow{\mathrm{H^+}} \mathrm{Ar_3}\ (\mathbf{2c}, 40\%) + \mathrm{Ar_2}p\text{-}\mathrm{ClC_6H_4}\ (\mathbf{2k}, 60\%) \quad (5)$$

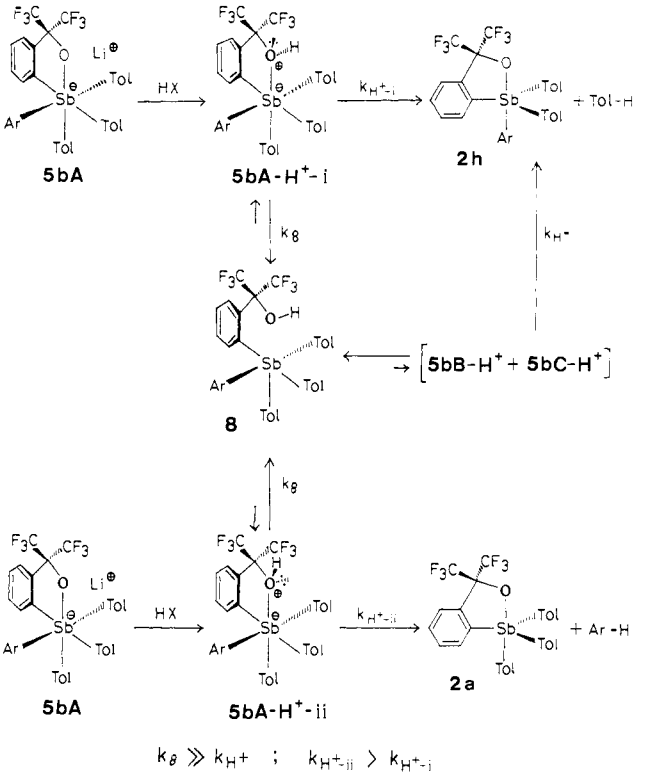
Reactivity ratios of carbon–Sb bonds are calculated from each result: i.e., from (1), Tol–Sb:Ar–Sb = 1.0:2.1; from (2), Tol–Sb:An–Sb = 1.0:4.9; from (3), Ar–Sb:Tol–Sb = 1.9:1.0; from (4), Ar–Sb:An–Sb = 1.0:2.8; from (5), Ar–Sb:*p*-ClC_6H_4–Sb = 1.0:2.0. It is remarkable that the result of (1) and (3) essentially coincided each other (1.9 ≒ 2.1) and a very close value could be obtained for Tol–Sb:An–Sb = 1.0:5.3 (≒4.9) from (3) and (4). Hence, the reactivity orders of **5A**-type complexes for protonolysis become as follows: An–Sb:*p*-ClC_6H_4–Sb:Ar–Sb:Tol–Sb ≒ 5:4:2:1. The orders of electronic effect of the substituent cannot be explained on the basis of only one factor, but there is a general trend that a carbon–Sb bond with a more electronegative group is more susceptible for protonolysis (the reason for the high reactivity of the *p*-$MeOC_6H_4$ group is not clear).

Table VI. Quenching of Mixtures of **5b** with Acetic Acid[a]

entry	ratio of ate complexes **5bA**:**5bB**:**5bC**	ratio of products **2a**:**2h**
1	43:20:37	37.4:62.6
2	32:27:41	36.9:63.1
3	32:28:40	39.8:60.2
4	27:40:33	32.8:67.2
5	25:49:26	33.5:66.5
6	22:54:24	37.9:62.1

[a] With 100 equiv of acetic acid at room temperature.

Scheme VIII



$k_B \gg k_{H^+}$; $k_{H^+\text{-ii}} > k_{H^+\text{-i}}$

Direct protonolysis of the carbon–Sb bond cannot be accepted because there was no effect of acidity of any protic acid. Protonation should take place at the lone-pair electrons of the oxygen atom to afford **5bA**-H^+-i and **5bA**-H^+-ii in an equal amount and the oxygen–Sb bond is cleaved to give **8** as a main product, where a small amount of final product is also produced ($k_8 \gg k_{H^+}$). Because Berry pseudorotation in **8** is very fast, a mixture of three kinds of ate complexes is formed in equilibrium with **8**, from which final products (**2a** + **2h**) are formed. Hydrocarbon is produced by syn elimination, and $k_{H^+\text{-ii}}$ should be larger than $k_{H^+\text{-i}}$ because the Ar group is more electron-withdrawing than the Tol group.[29] Relative rate of intramolecular ring-opening to hydrocarbon

(27) Cote, G.; Bauer, D. *J. Chem. Res. (S)* **1977**, 206. Day, M. C.; Medley, J. H.; Ahmad, N. *Can. J. Chem.* **1983**, *61*, 1719.
(28) Stevenson, W. H., III; Wilson, S.; Martin, J. C.; Fahnham, W. B. *J. Am. Chem. Soc.* **1985**, *107*, 6340.
(29) DePuy, C. H.; Bierbaum, V. M.; Damrauer, R. *J. Am. Chem. Soc.* **1984**, *106*, 4051. Davis, L. P.; Burggraf, L. W.; Gordon, M. S. *J. Am. Chem. Soc.* **1988**, *110*, 3056.

elimination should be quite large ($k_s \gg k_{H^+}$) because relative reactivities for protonolysis of the Tol–Sb bond and the Ar–Sb bond from **5bA**, **5bB**, and **5bC** are rather close to each other and also because the Ar–Sb bond is cleaved even from **5bB**, in which Ar group is trans to the oxygen atom. The intermediate **8** could not be observed even if **5bA** was quenched at −50 °C. In the case of **5a**, direct protonolysis of the carbon–Sb bond should take part to some extent because there were observed certain effects of acid strength and steric hindrance.

Experimental Section

Melting points were taken on a Yanagimoto micro melting point apparatus and were uncorrected. ^1H (90-MHz), ^{13}C (23-MHz), and ^{19}F (85-MHz) NMR spectra were recorded on a Hitachi R-90H spectrometer. The 470-MHz ^{19}F NMR spectra were recorded on a JEOL GX-500 spectrometer. Chemical shifts are reported (δ scale) from internal tetramethylsilane for ^1H and ^{13}C, or from external fluorotrichloromethane for ^{19}F. Mass spectra were recorded on a Hitachi RMU-6L spectrometer. Flash column chromatography was carried out on Merck silica gel 60, 230–400 mesh. Thin-layer chromatography (TLC) was performed with Merck silica gel GF-254 plates. Ab initio calculation was carried out by HITAC M-680H computer at the Institute for Molecular Science.

Solvents and Reagents. The preparation of lithium 1,1,1,3,3,3-hexafluoro-2-(2-lithiophenyl)-2-propoxide (**3**) from *n*-BuLi, 10% *N,N,N',N'*-tetramethylethylenediamine (TMEDA), and the corresponding alcohol followed published procedures.[11] Triphenylantimony[24] and tris(*p*-methylphenyl)antimony[25] dibromides were prepared by published procedures. Tris[*p*-(trifluoromethyl)phenyl]antimony dibromide (mp 143–144.5 °C) was prepared from the corresponding stibine[26] and bromine. Trimethylantimony dichloride[27] was prepared from antimony trichloride and methylmagnesium iodide, followed by distillation and reaction with excess of sulfuryl chloride. Ether and tetrahydrofuran (THF) were distilled from sodium–benzophenone.

Preparation of 2. General Procedure. To a solution of **3** (15.0 mmol) in THF–*n*-hexane was added a solution of triarylantimony dibromide (or trimethylantimony dichloride) (10 mmol) in 35 mL of THF at 0 °C with stirring under N_2. The mixture was stirred for 20 h at room temperature and quenched with cold water. Extraction with ether (3 × 60 mL), drying ($MgSO_4$), and removal of the ether gave crude **2**. Recrystallization from benzene or flash column chromatography (ethyl acetate–*n*-hexane) gave colorless crystals of **2**.

3,3-Bis(trifluoromethyl)-1,1,1-tris(*p*-methylphenyl)-3*H*-2,1-benzoxastibole (2a): yield 71%; mp 192–193 °C; ^1H NMR ($CDCl_3$) 2.37 (s, 9 H), 7.05–7.70 (m, 3 H), 7.20 (d, 6 H, J = 8 Hz), 7.47 (d, 6 H, J = 8 Hz), 7.93 (br, 1 H, J = 8 Hz); ^{19}F NMR (THF) −75.0 (s, 6 F at 25 °C), −75.1 (s, 6 F at −50 °C); ^{13}C NMR (THF) 22.0 (q), 78.7 (septet), 125.2 (q), 128.2 (d), 130.1 (d), 130.7 (d), 132.7 (s), 132.8 (d), 135.5 (d), 135.8 (s), 136.0 (d), 139.1 (s), 141.0 (s); MS, m/z (relative intensity) 637 ($M^{+\cdot}$, 2), 618 ($M^{+\cdot}$ − F, 3), 568 ($M^{+\cdot}$ − CF_3, 7), 546 ($M^{+\cdot}$ − $CH_3C_6H_4$, 100). Anal. Calcd for $C_{30}H_{25}F_6OSb$: C, 56.54; H, 3.95. Found: C, 56.79; H, 3.94.

3,3-Bis(trifluoromethyl)-1,1,1-triphenyl-3*H*-2,1-benzoxastibole (2b): yield 39%, mp 196–199 °C; ^1H NMR (C_6D_6) 6.98–7.73 (m, 18 H), 8.10 (br, 1 H, J = 8 Hz). Anal. Calcd for $C_{27}H_{19}F_6OSb$: C, 54.49; H, 3.22. Found: C, 54.62; H, 3.15.

3,3-Bis(trifluoromethyl)-1,1,1-tris[*p*-(trifluoromethyl)phenyl]-3*H*-2,1-benzoxastibole (2c): yield 48%; mp 175–177 °C; ^1H NMR ($CDCl_3$) 7.14–7.81 (m, 15 H), 8.04 (br, 1 H, J = 8 Hz); ^{19}F NMR (THF) −75.2 (s, 6 F), −63.8 (s, 9 F). Anal. Calcd for $C_{30}H_{16}F_{15}OSb$: C, 45.09; H, 2.02. Found: C, 45.30; H, 2.03.

3,3-Bis(trifluoromethyl)-1,1,1-trimethyl-3*H*-2,1-benzoxastibole (2d): yield 33%, mp 103–109 °C; ^1H NMR ($CDCl_3$) 1.38 (s, 9 H), 7.50–7.75 (m, 3 H), 7.90 (br, 1 H, J = 7 Hz); ^{19}F NMR (THF) −76.7 (s, 6 F). Anal. Calcd for $C_{12}H_{13}F_6OSb$: C, 35.24; H, 3.20. Found: C, 35.25; H, 3.00.

Attempted Reactions of 2a. (i) White crystals of **2a** were heated to 240–250 °C for 3 h, but 84% of **2a** was recovered after TLC. (ii) A solution of **2a** (0.05 mmol) and $(NH_4)_2Ce(NO_3)_6$ (0.09 mmol) in 306 mg of C_6D_6 and 219 mg of CD_3CN was heated to 60 °C for 10 h. **2a** (87%) was recovered after TLC. (iii) A solution of **2a** (0.025 mmol) and $CH_2{=}N^+Me_2I^-$[28] (0.04 mmol) in 0.5 mL of $(CD_3)_2SO$ was heated to 60 °C for 3 days. **2a** (64%) was recovered from extraction of *n*-hexane. (iv) A solution of **2a** (0.04 mmol) and EtCOCl (0.38 mmol) in 0.5 mL of C_6D_6 was heated to 60 °C for 1 day. **2a** was recovered quantitatively after evaporation of the solvent.

3,3-Bis(trifluoromethyl)-1-chloro-1,1-bis(*p*-methylphenyl)-3*H*-2,1-benzoxastibole (4a). To a solution of **2a** (0.16 mmol) in 3 mL of CH_2Cl_2 was added 0.06 mL of sulfuryl chloride (0.8 mmol) at room temperature with stirring. After 2 h of stirring, the mixture was evaporated. The residue was recrystallized from ether–*n*-hexane to give colorless crystals: yield 90%; mp 151–152 °C; ^1H NMR ($CDCl_3$) 2.37 (s, 6 H), 7.6–7.9 (m, 3 H), 7.30 (d, 6 H, J = 8 Hz), 8.04 (d, 6 H, J = 8 Hz), 8.68 (dd, 1 H, J = 6.6, 2.4 Hz); ^{19}F NMR ($CDCl_3$) −75.0 (s, 6 F). Anal. Calcd for $C_{23}H_{18}ClF_6OSb$: C, 47.50; H, 3.12. Found: C, 47.25; H, 3.10.

3,3-Bis(trifluoromethyl)-1-bromo-1,1-bis(*p*-methylphenyl)-3*H*-2,1-benzoxastibole (4b). To a solution of **2a** (10 mmol) in 10 mL of $CHCl_3$ was added 1 equiv of bromine at room temperature with stirring. After 10 min of stirring, the mixture was evaporated. The residue was recrystallized from benzene to give colorless crystals: yield 82%; mp 136.5–137.0 °C; ^1H NMR ($CDCl_3$) 2.37 (s, 6 H), 7.5–8.0 (m, 3 H), 7.29 (d, 4 H, J = 8 Hz), 8.01 (d, 4 H, J = 8 Hz), 8.73 (br, 1 H, J = 8 Hz); ^{19}F NMR ($CDCl_3$) −75.1 (s, 6 F). Anal. Calcd for $C_{23}H_{18}BrF_6OSb$: C, 44.13; H, 2.90. Found: C, 44.42; H, 2.85.

Detection and Measurement of the Isomerization Rate of 5a. In a typical run, to a solution of **2a** (100.6 mg, 0.158 mmol) in 11 mL of THF at −78 °C was added with stirring under N_2 1 equiv of methyllithium (1.5–1.6 M ether solution). After 10 min of stirring, 0.4 mL of the solution was transferred to a precooled NMR tube at that temperature under N_2. ^{19}F NMR of the solution showed a pair of quartets [**5aA**: δ −74.2 and −74.8 (q × 2, $^4J_{F-F}$ = 9 Hz)] at −50 °C. At −20 °C the composition of isomers [**5aA** and **5aB**: δ −73.8, (s)] was conveniently monitored by integration of the CF_3 signals. Equilibrium was attained within 90 min (**5aA**:**5aB** = 3.8:1.0). The kinetic data were analyzed by reversible first-order kinetics, and then least-squares analyses provided the following value (average value of rate constants in five experiments); $k_{isom} = (1.8 \pm 0.1) \times 10^{-4}$ s^{-1} (−20 °C).

Detection and Isomerization of 5b. In a typical run, to a solution of **2a** (90 mg, 0.14 mmol) in 9 mL of THF at −78 °C was added with stirring under N_2 1 equiv of *p*-$CF_3C_6H_4Li$ (0.14 M hexane solution). After 10 min of stirring, ca. 0.4 mL of the solution was transferred to a precooled NMR tube at that temperature. ^{19}F NMR (85 MHz) of the solution showed a singlet (δ −73.8) for CF_3 groups on the bidentate ligand and three singlets for $CF_3C_6H_4$ group (δ −62.1:−62.2:62.6 = 98:1:1 at −50 °C). The ratio of the three singlets was constant at −50, −20, and 0 °C. Isomerization took place slowly at 25 °C, and the composition was monitored by the $CF_3C_6H_4$ signals (initial ratio at 25 °C, δ −62.2:−62.1:−62.6 = 98:1:1). After 36 h the ratio changed to 83:12:5. The 470-MHz ^{19}F NMR of the solution showed a pair of quartets and two singlets for CF_3 groups on the bidentate ligand, the ratio of which [83:11:6 (δ −73.75 and −73.85 (q), −73.65 (s), −73.70 (s)] was consistent with that of $CF_3C_6H_4$ group observed by 85-MHz ^{19}F NMR.

Substituent Effect of the Para-Substituted Phenyl Group on the ^{19}F NMR Chemical Shift of 5. In a typical run, to a solution of **2c** (82 mg, 0.10 mmol) in 6.5 mL of THF was added 1 equiv of *p*-$CH_3C_6H_4Li$ (0.14 M hexane solution) with stirring under N_2 at room temperature. After 10 min of stirring, ca. 0.5 mL of the solution was transferred to an NMR tube under N_2. ^{19}F NMR of the solution showed three singlets of the $CF_3C_6H_4$ group.

Reaction of 2a with Methyllithium and Quenching of 5a with Water *in an NMR Tube*. To a solution of **2a** (20–40 mg) in 0.5 mL of THF *in an NMR tube* was added methyllithium (20% excess of a 1.3–1.6 M ether solution) at room temperature without stirring under N_2. After 30 min, the mixture was quenched with water to give **2e**, **2f**, and **2a** in a ratio of 84:11:5. The products were determined by TLC separation.

3,3-Bis(trifluoromethyl)-1-methyl-1,1-bis(*p*-methylphenyl)-3*H*-2,1-benzoxastibole (2e): mp 176–178 °C; ^1H NMR ($CDCl_3$) 1.90 (s, 3 H), 2.40 (s, 6 H), 6.85–7.65 (m, 3 H), 7.23 (d, 4 H, J = 8 Hz), 7.44 (d, 4 H, J = 8 Hz), 7.92 (br, 1 H, J = 8 Hz); ^{19}F NMR (THF) −75.5 (s, 6 F). Anal. Calcd for $C_{24}H_{21}F_6OSb$: C, 51.37; H, 3.77. Found: C, 51.55; H, 3.78.

3,3-Bis(trifluoromethyl)-1,1-dimethyl-1-(*p*-methylphenyl)-3*H*-2,1-benzoxastibole (2f): mp 115–118 °C; ^1H NMR ($CDCl_3$) 1.77 (s, 6 H), 2.41 (s, 3 H), 7.05–7.70 (m, 3 H), 7.28 (d, 2 H, J = 8 Hz), 7.42 (d, 2 H, J = 8 Hz), 7.88 (br, 1 H, J = 8 Hz); ^{19}F NMR (THF) −76.4 (s, 6 F). Anal. Calcd for $C_{18}H_{17}F_6OSb$: C, 44.57; H, 3.53. Found: C, 44.64; H, 3.43.

Measurement of the Rate of Quenching of 1a with EtOH. To the equilibrium mixture of **5aA** and **5aB** described above in an NMR tube was added 0.146 mL of a solution of EtOH (0.46 mL, 0.788 mmol) in 1.0 mL of THF. The rate of formation of **2a** and **2e** and that of decrease of **5aA** and **5aB** were measured by ^{19}F NMR. The data were analyzed by pseudo-first-order kinetics and then least-squares analyses provided the following result (average value of rate constants in three experiments); $k_{quench} = (1.9 \pm 0.1) \times 10^{-5}$ L·mol^{-1}·s^{-1} (−20 °C).

Measurement of the Isomerization Rate in the Presence of Additives. To a solution of **5aA** transferred in an NMR tube as described above was added 10 equiv of HMPA [12-crown-4 or TMEDA (21 equiv)]. The composition of **5aA** and **5aB** was monitored by ^{19}F NMR.

Reaction of 2a with Methyllithium and Quenching of 5a with Protic Acids (or Protic Solvents) *in a Flask*. To a solution of **2a** (100 mg, 0.16 mmol) in 10 mL of THF *in a flask* was added methyllithium (20% excess of a 1.3-1.6 M ether solution) at room temperature with stirring under N_2. After 30 min of stirring, the mixture was quenched with 5-10 equiv of protic acids. The products were separated by TLC (ethyl acetate-*n*-hexane), and the ratio of **2a** to **2e** was determined by integration of CF_3 signals.

Protonolysis of 5bA with Various Protic Acids. To a solution of **2a** (150 mg, 0.24 mmol) in 15 mL of THF at room temperature was added 1.1 equiv of *p*-$CF_3C_6H_4Li$ (0.14 M hexane solution) with stirring under N_2 at room temperature. After 10 min of stirring, ca. 0.5 mL of the solution was transferred to an NMR tube and quenched with 100 equiv of protic acids. The ratio of **2a** to **2h** was calculated from the $CF_3C_6H_4$ signal of **2h** and the CF_3 signal (bidentate ligand) of **2a** and **2h**. The products were determined by TLC separation.

3,3-Bis(trifluoromethyl)-1,1-bis(*p*-methylphenyl)-1-[*p*-(trifluoromethyl)phenyl]-3*H*-2,1-benzoxastibole (2h): mp 182.5-183.5 °C; ^1H NMR ($CDCl_3$) 2.37 (s, 6 H), 7.24 (d, 4 H, J = 8 Hz), 7.10-8.10 (m, 8 H); ^{19}F NMR (THF) -75.0 (s, 6 F), -63.7 (s, 3 F). Anal. Calcd for $C_{30}H_{22}F_9OSb$: C, 52.13; H, 3.21. Found: C, 51.87; H, 3.20.

Protonolysis of a Mixture of 5b with 100 equiv of Acetic Acid. To a solution of **2h** (116 mg, 0.17 mmol) in 10.7 mL of THF was added 1 equiv of *p*-$CH_3C_6H_4Li$ (1.27 M ether solution) with stirring under N_2 at 0 °C. After 5 min of stirring, ca. 0.5 mL of the solution was transferred to an NMR tube at appropriate time intervals. The ratio of the three ate complexes (**5bA**:**5bB**:**5bC**) was measured by ^{19}F NMR, and the solution was quenched with 100 equiv of acetic acid. The ratio of **2a** to **2h** was determined by ^{19}F NMR.

Protonolysis of 5cA, 5dA, 5eA, and 5gA with 100 equiv of Acetic Acid or a Large Excess of Water. To a solution of **2c** (103 mg, 0.13 mmol) in 3 mL of ether was added 1.5 equiv of *p*-$CH_3C_6H_4Li$ with stirring under N_2 at -78 °C. After 30 min of stirring at room temperature the mixture was quenched with 100 equiv of acetic acid or a large excess of water. The ratio of **2c** to **2g** was determined by ^{19}F NMR and/or HPLC analysis. The products were separated by TLC (chloroform-*n*-hexane 3:8).

3,3-Bis(trifluoromethyl)-1-(*p*-methylphenyl)-1,1-bis[*p*-(trifluoromethyl)phenyl]-3*H*-2,1-benzoxastibole (2g): mp 166.5-169 °C; ^1H NMR ($CDCl_3$) 2.40 (s, 3 H), 7.28 (d, 2 H, J = 8 Hz), 7.49 (d, 2 H, J = 8 Hz), 7.12-8.04 (m, 12 H); ^{19}F NMR (THF) -75.0 (s, 6 F), -63.8 (s, 6 F). Anal. Calcd for $C_{30}H_{19}F_{12}OSb$: C, 48.35; H, 2.57. Found: C, 48.33; H, 2.60.

3,3-Bis(trifluoromethyl)-1-(*p*-methoxyphenyl)-1,1-bis(*p*-methylphenyl)-3*H*-2,1-benzoxastibole (2i): mp 169.5-170.0 °C; ^1H NMR ($CDCl_3$) 2.37 (s, 6 H), 3.82 (s, 3 H), 6.94 (d, 2 H, J = 9 Hz), 7.20 (d, 4 H, J = 8 Hz), 7.45 (d, 4 H, J = 8 Hz), 7.55 (d, 2 H, J = 9 Hz), 7.3-8.0 (m, 4 H). Anal. Calcd for $C_{30}H_{25}F_6O_2Sb$: C, 55.16; H, 3.86. Found: C, 54.92; H, 3.78.

3,3-Bis(trifluoromethyl)-1-(*p*-methoxyphenyl)-1,1-bis[*p*-(trifluoromethyl)phenyl]-3*H*-2,1-benzoxastibole (2j): mp 113.5-115 °C; ^1H NMR ($CDCl_3$) 3.84 (s, 3 H), 6.99 (d, 2 H, J = 9 Hz), 7.57 (d, 2 H, J = 9 Hz), 7.0-8.0 (m, 12 H); ^{19}F NMR ($CDCl_3$) -74.6 (s, 6 F), -63.4 (s, 6 F). Anal. Calcd for $C_{30}H_{19}F_{12}O_2Sb$: C, 47.34; H, 2.52. Found: C, 47.63; H, 2.48.

3,3-Bis(trifluoromethyl)-1-(*p*-chlorophenyl)-1,1-bis[*p*-(trifluoromethyl)phenyl]-3*H*-2,1-benzoxastibole (2k): mp 159.5-161 °C; ^1H NMR ($CDCl_3$) 7.69 (s, 8 H), 7.0-8.1 (m, 8 H); ^{19}F NMR ($CDCl_3$) -74.7 (s, 6 F), -63.5 (s, 6 F). Anal. Calcd for $C_{29}H_{16}OF_{12}ClSb$: C, 45.49; H, 2.11. Found: C, 45.58; H, 2.15.

Acknowledgment. We are indebted for partial support of this research to Grant-in-Aid for Special Project Research (No. 61225019 and 62215026) administered by the Ministry of Education, Science and Culture of the Japanese Government. Also we are grateful to Professor J. C. Martin (Vanderbilt University) and Professor H. J. Reich (University of Wisconsin, Madison) for their helpful discussions, to Yuka Sunaguchi for preparation and some reactions of **2a** and **2b**, to Akira Mizuno and Yurimasa Zenitani for measurement of 470-MHz ^{19}F NMR, to Dr. Katsuya Kanda and Dr. Unpei Nagashima for calculation of antimony ate complexes, to Hideharu Iwasaki for calculation by least-squares methods, to Central Glass Co. Ltd. for the gift of hexafluorocumyl alcohol, and to the Computer Center, Institute for Molecular Science, Okazaki National Research Institute for the use of the HITAC M-680H computer.

Formation and Reaction of the Quinone Methide from Reductive Cleavage of the Antitumor Drug Menogaril[1]

Marybeth Boldt, Giorgio Gaudiano, Makhluf J. Haddadin,[2] and Tad H. Koch*

Contribution from the Department of Chemistry and Biochemistry, University of Colorado, Boulder, Colorado 80309-0215. *Received August 5, 1988*

Abstract: Anaerobic reduction of menogaril (**1**), a semisynthetic antitumor drug in clinical trials, with *d,l*-bi(3,5,5-trimethyl-2-oxomorpholin-3-yl) (TM-3 dimer) in methanol gave 7-deoxynogarol (**5**) and stereoisomers of bi(7-deoxynogarol-7-yl) (**6**) and, in the presence of *N*-acetylcysteine, 7-(*N*-acetylcysteinyl)-7-deoxynogarol (**10**) via an observed quinone methide intermediate (**8**). In the presence of excess reducing agent, **5** was formed relatively rapidly as the major product in its hydroquinone state. The rate-controlling step, tautomerization of the quinone methide, was autocatalyzed; the product, the hydroquinone of **5**, catalyzed the reaction. In fact, several anthracycline-derived hydroquinones were effective catalysts. Uncatalyzed tautomerization of the quinone methide yielded little if any **5**, in contrast with facile unimolecular formation of 7-deoxyaglycons from reduction of other anthracyclines. In the absence or presence of excess reducing agent, the rate of formation of **6** or formation of **6** in its bishydroquinone state, respectively, was second order in quinone methide concentration and relatively slow. The rate constants for the autocatalyzed tautomerization and the dimerization of the quinone methide are 27 ± 2 and 11 ± 1 M^{-1} s^{-1}, respectively. Reduction of menogaril in aqueous medium gave predominantly 7-deoxynogarol (**5**) relatively rapidly with excess reducing agent and a mixture of **5** and the aglycon dimer **6** slowly with substoichiometric amounts of reducing agent. Under both sets of conditions, the quinone methide transient was not observed. Reduction in aqueous medium with 0.3 equiv of reducing agent in the presence of *N*-acetylcysteine gave high yields of adduct **10**, suggesting a relatively long lifetime for the unobservable quinone methide transient even in aqueous medium in the absence of hydroquinones and reactive nucleophiles. A possible in vivo consequence of the relatively slow uncatalyzed tautomerization of the quinone methide is efficient nucleophilic trapping.

Menogaril, 7-*con*-O-methylnogarol (**1**), is a semisynthetic antitumor drug of the anthracycline class synthesized from nogalamycin, a product of the organism *Streptomyces nogalater*.[3] The molecular structure and absolute stereochemistry result from

0002-7863/89/1511-2283$01.50/0