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Rapid Communication

Synthesis and Reactions of Conformational Isomers of a Stable Selenenic Acid Bearing a Bridged Calix[6]arene Framework

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ABSTRACT: *A stable selenenic acid bearing a bridged calix[6]arene framework fixed in the 1,2,3-alternate conformation was synthesized. Its properties were compared with those of its conformational isomer fixed in the cone conformation, indicating that the reactivity of the endohedral SeOH group can be regulated by the conformation of the calix[6]arene framework.* © 2001 John Wiley & Sons, Inc. Heteroatom Chem 12:195–197, 2001

Dedicated to Professor Naoki Inamoto on the occasion of his 72nd birthday.

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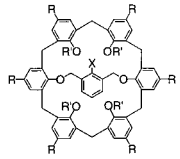
INTRODUCTION

Although selenenic acids (RSeOH) have been well recognized as important intermediates in organic and biochemical reactions of selenium compounds, the elucidation of their chemistry has been hampered by the absence of a methodology to get a stable compound of this species [1]. We investigated the development of the bridged calixarenes represented by the general formula **1** [2] and successfully applied it to the synthesis of the first isolable selenenic acid **2a** [3]. A stable selenenic acid bearing a 9-triptycyl group was also recently reported [4]. When calix[6]arenes are used as a molecular platform, it is often problematic that their conformational flexibility is very large [5]. We have found, however, that in the case of the bridged calix[6]arenes **1**, two conformationally frozen isomers, that is, the cone isomer and the 1,2,3-alternate isomer, can be easily obtained by arylmethylation of the four hydroxy groups at the lower rim [6]. Selenenic acid **2a**, bearing four benzyloxy groups at the lower-rim, is fixed in the cone conformation. It is very intriguing how the properties of the functional group embedded in the cavity are regulated by the conformation of the calix[6]arene framework. Here we report the synthesis of a selenenic acid **2c** bearing the 1,2,3-alternate conformation and the relationship between the proper-

ties of the SeOH functionality and the conformation of the molecule.



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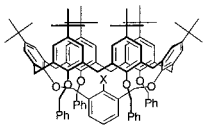
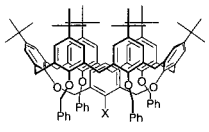
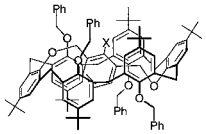


Ar^1X (cone with upward X)
2a (X = SeOH)
5a (X = SeO_2H)
6a (X = $SeSBu^n$)



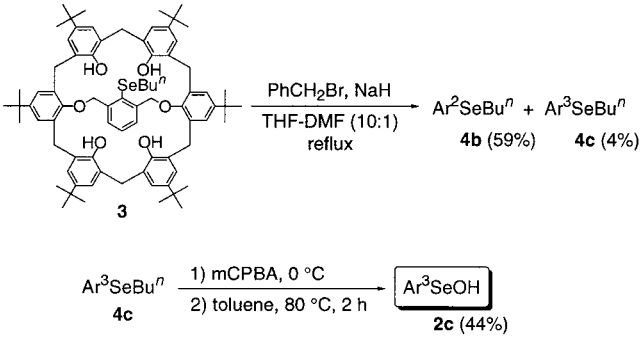
Ar^2X (cone with downward X)
4b (X = $SeBu^n$)



Ar^3X (1,2,3-alternate)
2c (X = SeOH)
4c (X = $SeBu^n$)
5c (X = SeO_2H)

RESULTS AND DISCUSSION

The butyl selenide **4c** bearing the 1,2,3-alternate conformation was prepared by the reaction of the tetrahydroxy compound **3** with benzyl bromide in the presence of NaH followed by chromatographic separation from the cone isomer **4b** (Scheme 1), although the isolated yield of **4c** (4%) was much lower than that of **4b** (59%) [7]. Oxidation of selenide **4c** with *m*-chloroperbenzoic acid (mCPBA) followed by thermolysis in toluene at 80°C afforded selenenic acid **2c** with the 1,2,3-alternate conformation, which was isolated by silica gel chromatography as colorless crystals in 44% yield [8]. Selenenic acid **2c** showed high stability both in the crystalline state and in solution, similarly to the cone isomer **2a**. Even after heating at 120°C for 5 hours in $CDCl_2CDCl_2$, **2c** underwent only slight decomposition. Some spectral data of **2c** are shown in Table 1 together with those of **2a**. The OH absorption bands of **2a** and **2c** in the IR spectra suggest that there are

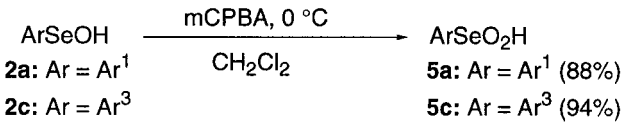


SCHEME 1

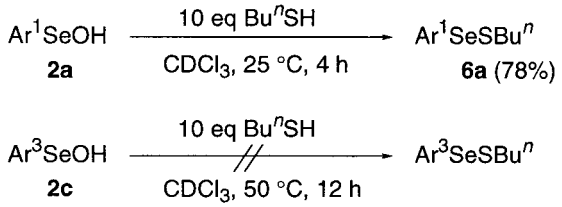
TABLE 1 Spectral Data of Selenenic Acids **2a** and **2c**

	δ_H (OH)[a]	δ_{Se}[a]	ν(OH)/cm^{-1}[b]
2a[c]	−0.05	1133.8	3523
2c	4.34	1097.5	3392

[a]In $CDCl_3$.
[b]In CH_2Cl_2.
[c]Ref. [3].



SCHEME 2



SCHEME 3

intramolecular hydrogen bonding interactions in the latter while no significant interaction of such kind exists in the former. This interpretation is supported by observation of the ^1H NMR signal due to the hydroxy proton of **2c** appearing at a much lower field than that of **2a**, even if it is taken into account that the OH group of **2a** is likely to be more highly shielded by the calix[6]arene macroring. Apparently, in these two kinds of isomers, the calix[6]arene macroring of each conformation provides a considerably different environment for the SeOH functionality, although both of them stabilize this otherwise unstable species effectively (See Table 1).

Both conformational isomers **2a** and **2c** reacted with mCPBA to afford the corresponding seleninic acids **5a** and **5c**, respectively (Scheme 2). On the other hand, they showed different reactivities toward a thiol. While the cone isomer **2a** reacted with an excess amount of 1-butanethiol at room temperature to give selenenyl sulfide **6a**, the 1,2,3-alternate isomer **2c** underwent no reaction even at 50°C (Scheme 3). This result can be explained by assuming that the intramolecular hydrogen bonding of the OH group of **2c** reduces the electrophilicity of the Se atom of the SeOH group, although the steric congestion around the SeOH group may also be responsible. These results clearly demonstrate that the

reactivity of the endohedral functionality can be regulated by the conformation of the calix[6]arene framework.

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[7] The structure of **4b** was determined by X-ray crystallographic analysis, the details of which will be reported elsewhere.

[8] **2c**: colorless crystals; m.p. 103–110°C (dec); ^{1}H NMR (500 MHz, $CDCl_3$, TMS, 57°C) δ 0.98 (s, 18H, *t*-Bu), 1.00 (s, 18H, *t*-Bu), 0.98 (s + s, 9 + 9H, *t*-Bu), 3.26 (d, ^{2}J = 15.9 Hz, 2H, $ArCH_2Ar$), 3.34 (d, ^{2}J = 15.6 Hz, 2H, $ArCH_2Ar$), 3.72 (d, ^{2}J = 13.0 Hz, 2H, $ArCH_2Ar$), 3.74 (d, ^{2}J = 13.0 Hz, 2H, $ArCH_2Ar$), 3.99 (d, ^{2}J = 15.9 Hz, 2H, $ArCH_2Ar$), 4.05 (s, 1H, SeOH), 4.06 (dd, ^{3}J = 7.6 Hz, ^{4}J = 1.5 Hz, 1H, arom), 4.22 (s, 2H, $ArOCH_2Ar$), 4.35 (s, 2H, $ArCH_2OAr$), 4.61 (d, ^{2}J = 15.6 Hz, 2H, $ArCH_2Ar$), 4.65 (d, ^{2}J = 11.0 Hz, 2H, $PhCH_2O$), 4.72 (d, ^{2}J = 10.4 Hz, 2H, $PhCH_2O$), 4.78 (d, ^{2}J = 11.0 Hz, 2H, $PhCH_2O$), 5.00 (d, ^{2}J = 10.4 Hz, 2H, $PhCH_2O$), 6.18 (dd, ^{3}J = 7.6, 7.5 Hz, 1H, arom), 6.69 (br d, 2H), 6.80 (dd, ^{3}J = 7.5 Hz, ^{4}J = 1.5 Hz, 1H), 6.83 (br d, 2H, arom), 6.94 (d, ^{4}J = 2.5 Hz, 2H), 7.07 (d, ^{4}J = 2.4 Hz, 2H), 7.13 (s, 2H), 7.14 (s, 2H), 7.31–7.60 (m, 20H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.6 (t), 28.9 (t), 31.2 (q), 31.3 (q), 31.58 (q), 31.62 (q), 34.03 (s), 34.05 (s), 34.14 (s × 2), 35.1 (t), 72.4 (t), 74.1 (t), 74.7 (t), 75.8 (t), 123.9 (d), 125.5 (d), 127.3 (d), 127.4 (d), 127.5 (d), 127.7 (d), 127.86 (s), 127.86 (d), 127.93 (d), 128.0 (d), 128.4 (d), 128.5 (s), 128.5 (d), 128.8 (d), 129.3 (d), 130.6 (d), 131.5 (s), 131.8 (d), 132.0 (s), 132.7 (s), 132.9 (s), 135.7 (s), 137.1 (s), 137.2 (s), 138.1 (s), 139.1 (s), 144.3 (s), 144.6 (s), 144.9 (s), 145.6 (s), 150.6 (s), 152.6 (s), 152.9 (s), 153.1 (s); ^{77}Se NMR (95 MHz, $CDCl_3$) δ 1097.5; IR (CH_2Cl_2) 3392 cm^{-1} (ν_{OH}). HRMS (FAB) found *m/z* 1530.7771 (M^+), calcd for $C_{102}H_{114}O_7{}^{80}Se$ 1530.7730.