1-(Organoselanyl)perfluoroalkanols: A Stable and Efficient Precursor for Organoselenols

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The 1-(organoselanyl)perfluoroalkanols **1**, **3**, **4**, and **10** were successfully prepared and reactions with hexanoyl chlorides to produce the corresponding esters **5**, **7**, and **8**, accompanied by the selenoesters **6** were conducted. The DBU-mediated alkylations of the heptafluorobutanols **4**, **10**, and the α-*p*-nitrobenzoate **2** with alkyl halides easily provided alkyl phenyl selenides **9a**–**9i** and **11a**–**11c** in good to high yields.

1-Organoselanylalkanols (1-organoselanyl hemiacetals) are recognized as labile intermediates in the syntheses of 1,1-bis(organoselanyl)alkanes (*Se*,*Se*-acetals) (Figure 1).[1] The corresponding sulfur analogs were reported to be isolated as 2,2,2-trifluoro-1-(organosulfanyl)ethanol by hydrolysis of the acetate; however, the yield of the product was very low.[2] Since a convenient and easy access to 1-organosulfanyl and selanylalkanols (sulfanyl and selanylhemiacetals) has not been reported, we conducted the syntheses of these analogs as perfluoroalkanols and now report the initial results of the selenium analogs and their unique reactivities.

First, we examined preparation of 1-(phenylselanyl)perfluoroalkanols as 1-organoselanyl hemiacetals (Scheme 1). We selected trifluoroacetaldehyde ethyl hemiacetal as the commercially available precursor of the selenohemiacetals and phenylselanyldiisobutylaluminum[3] as the soft selenium nucleophile. The reaction proceeded over 1 h to quantitatively give 2,2,2-trifluoro-1-(phenylselanyl)ethanol (**1**);[4] however, further purifications by chromatography afforded the diphenyl diselenide. Distillation afforded almost pure hemiacetal **1**, however, elemental analysis could not be accomplished because the material contained a small amount of benzeneselenol. The structure determination of **1** was based on the spectral data, which showed a doublet at δ 2.54 ($J = 9$ Hz) due to the hydroxy group and a doublet of quartets at δ 5.39 ($J = 9$ and 7 Hz) due to the α-proton of the

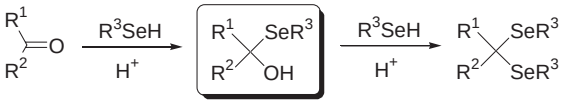
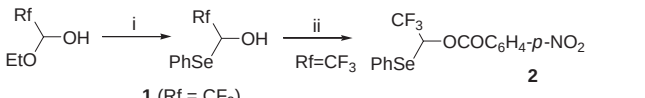


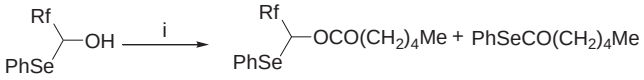
Figure 1. 1-Organoselanylalkanols (1-organoselanyl hemiacetals).



1 (Rf = CF_3)
3 (Rf = CF_3CF_2)
4 (Rf = $CF_3CF_2CF_2$)

Reagent: i, *i*-$Bu_2AlSePh$ (1.2 equiv), toluene, 0 °C, 1 h; ii, *p*-$NO_2C_6H_4COCl$ (1.2 equiv), pyridine (1.0 equiv), DMAP (0.1 equiv)

Scheme 1. Synthesis of 1-(organoselanyl)perfluoroalkanols.



1	**5** (Rf = CF_3)(55%)	**6** (17%)
3	**7** (Rf = CF_2CF_3)(43%)	**6** (49%)
4	**8** (Rf = $CF_2CF_2CF_3$)(15%)	**6** (68%)

Reagent: i, $Me(CH_2)_4COCl$ (1.2 equiv), pyridine (1.0 equiv), DMAP (0.1 equiv), CH_2Cl_2, 0 °C, 10 min

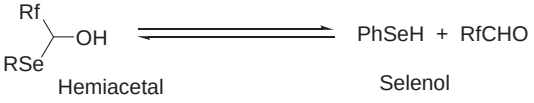
Scheme 2. Reactions of 1-(phenylselanyl)perfluoroalkanols **1**, **3**, and **4** with hexanoyl chloride.

selanyl group in the ^{1}H NMR spectrum, a singlet at δ 1.73 in the ^{19}F NMR spectrum, and m/z 256 (M^+) in the mass spectrum. Furthermore, the hemiacetal **1** was isolated as *p*-nitrobenzoate **2** (mp 75–76 °C). Hemiacetal **1** was also found to be very stable both in air for 8 months and in $CDCl_3$ for one week. We next prepared both 2,2,3,3,3-pentafluoro-1-(phenylselanyl)propanol (**3**) and 2,2,3,3,4,4,4-heptafluoro derivative **4** by almost the same procedure,[5] and performed reactions with hexanoyl chloride as shown in Scheme 2.

The reaction of trifluoroethanol **1** with hexanoyl chloride gave the 2,2,2-trifluoro-1-(phenylselanyl)ethyl hexanoate (**5**) in 55% yield, accompanied by *Se*-phenyl hexaneselenoate **6** in 17% yield. The hexanoylation reactions of both 2,2,3,3,3-pentafluoropropanol **3** and 2,2,3,3,4,4,4-heptafluorobutanol **4** surprised us based on the yields of the products. The yields of the esters **5**, **7**, and **8** decreased as the length of the perfluoroalkyl groups grew longer, while that of the selenoesters increased. In particular, the yield of **6** in the reaction of **4** with hexanoyl chloride is the highest. This tendency was observed in the reactions with isobutyryl chloride, benzoyl chloride, and *p*-bromobenzoyl chloride.

The reactivity could be explained by the relative K_a of the perfluoroalkanols **1**, **3**, and **4** under basic condition given in Figure 2. Since the distillates contain a small amount of benzeneselenol, the hemiacetals would be in equilibrium with both benzeneselenol and the perfluoroalkanols. The product ratios of the hexanoylations would be due to the acidities of the hydroxy groups of the hemiacetals, and the 2,2,3,3,4,4,4-heptafluorobutanol **4** was found to be useful for producing the benzeneselenol.

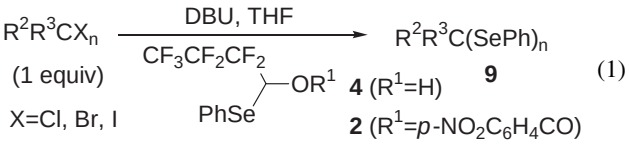
We found that 2,2,3,3,4,4,4-heptafluorohemiacetal **4** was a



Ka: $CF_3 < CF_2CF_3 < CF_2CF_2CF_3$

Figure 2. Relative K_a of 1-(organoselanyl)perfluoroalkanols in the presence of DBU.

good compound to provide benzeneselenol, therefore, we next tried to utilize hemiacetal **4** as the precursor of benzeneselenol. Benzeneselenol is the most common selenium compound and is commercially available or in situ generated from diphenyl diselenide/H_3PO_2 in THF–H_2O; however, it is highly labile in air and easily undergoes oxidation to form diphenyl diselenide.[6] There exist many reagents providing its synthetic equivalent, such as trimethylsilyl phenyl selenide (TMSSePh),[7] tris(phenylselanyl)borane ($B(SePh)_3$),[8] sodium and lithium benzeneselenolate PhSeM,[9] *i*-$Bu_2AlSePh$,[3] $(PhSe)_2/NaBH_4$,[10] and $(PhSe)_2/LiAlH_4$.[11] The metal organoselenolates[9] have sometimes acted as effective reducing agents, not as nucleophiles.[7b] Organoselenols generated from the hemiacetals would be a powerful tool for the selective introduction of selenium functional groups. Therefore, we next performed alkylations of hemiacetal **4** with alkyl halides. First, a productive approach was to change the base in the reaction of **4** with benzyl bromide under conditions such as 1 equiv of base at 0 °C for 10 min. Reaction in the presence of 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) afforded **9e** in 66% yield, however, the other bases were ineffective for the alkylation as follows: pyridine/DMAP (0.1 equiv) in 29%, 1 mol/L NaOH in 32%, *i*-Pr_2NEt in 49%, triethylamine in 29% yield. Since DBU was found to be the most suitable for removing benzeneselenol from **4**, we next examined the reactions with some alkyl halides and the results are shown in Table 1. Since we found that aroyloxyperfluoroalkanes **2** also decomposed in the presence of DBU, we further investigated alkylations using **2** and obtained alkyl phenyl selenides **9c**–**9f** and **9i** in good to high yields (Entries 11–15).



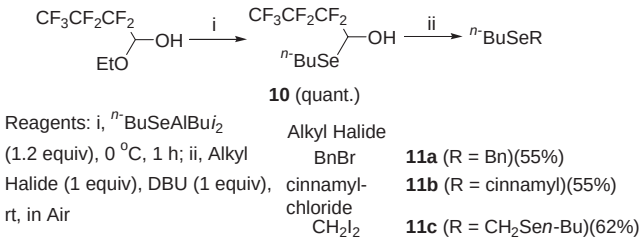
(1)

We next examined the preparations of the other hemiacetal bearing butylselanyl group (Scheme 3). Since butylselanyl derivative **10** was quantitatively obtained, we also examined the

Table 1. Base-mediated alkylation of 2,2,3,3,4,4,4-heptafluorobutanol **4** and *p*-nitrobenzoate **2**

Run	Acetal (equiv)	Alkyl halide $R^2R^3CX_n$	Conditions[a,b]	Yield of **9**/%[c]
1	**4** (1)	MeI	rt, 2 h	**9a** (68)
2	**4** (1)	EtI	rt, 10 min	**9b** (56)
3	**4** (1)	*i*-PrI	rt, 0.5 h	**9c** (86)
4	**4** (1)	*n*-BuI	rt, 15 min	**9d** (quant)
5	**4** (1)	BnBr	0 °C, 1 h	**9e** (91)
6	**4** (1)	(*E*)-cinnamyl chloride	0 °C, 1 h	**9f** (84)
7	**4** (1)	Allyl bromide	rt, 2 h	**9g** (64)
8	**4** (1)	$TMSCH_2Cl$	0 °C, 0.5 h	**9h** (54)
9	**4** (2)	CH_2I_2	0 °C, 0.5 h	**9i** (70)
10	**4** (3)	$CHBr_3$	0 °C, 0.5 h	**9j** (66)
11	**2** (1)	*i*-PrI	rt, 30 min	**9c** (59)
12	**2** (1)	*n*-BuI	rt, 1 h	**9d** (64)
13	**2** (1)	BnBr	rt, 10 min	**9e** (quant)
14	**2** (1)	(*E*)-cinnamyl chloride	0 °C, 1 h	**9f** (68)
15	**2** (2)	CH_2I_2	rt, 1 h	**9i** (56)

[a]All reactions were carried out in air. [b]Equiv of DBU was shown as follows. Entries 1–8: 1 equiv; Entry 9: 2 equiv; Entries 11–15: 3 equiv; Entry 10: 3 equiv Entry 15: 6 equiv. [c]Isolated yields of **9**.



Scheme 3. Synthesis and alkylations of 1-butylselanyl-2,2,3,3,4,4,4-heptafluorobutanol (**10**).

DBU-promoted alkylations of the hemiacetal **10** with a few alkyl halides. Satisfactory results were obtained as shown in Scheme 3.

In summary, we have described for the first time the syntheses of 1-organoselanyl hemiacetals as perfluoroalkanols, which were isolated as alkanoyloxyalkanes or aroyloxyalkanes. The base-promoted alkylations with alkyl halides proceeded in good to high yields. Since the organoselenols have been attracting much attention as novel anchoring groups of monolayers on metals in the chemistry of molecular electronics,[12] this methodology could be a powerful tool for providing indispensable organoselenols when required.

References and Notes

1 *O*-Trimethylsilyl ether: W. Dumont, A. Krief, *Angew. Chem.* **1977**, *89*, 559.
2 K. Uneyama, M. Momota, K. Hayashida, T. Itoh, *J. Org. Chem.* **1990**, *55*, 5364.
3 A. P. Kozikowski, A. Ames, *J. Org. Chem.* **1978**, *43*, 2735; K. Maruoka, T. Miyazaki, M. Ando, Y. Matsumura, S. Sakane, K. Hattori, H. Yamamoto, *J. Am. Chem. Soc.* **1983**, *105*, 2831; T. Inoue, T. Takeda, N. Kambe, A. Ogawa, I. Ryu, N. Sonoda, *J. Org. Chem.* **1994**, *59*, 5824.
4 S. Piettre, C. De Cock, R. Merenyi, H. G. Viehe, *Tetrahedron* **1987**, *43*, 4309.
5 **4**: IR (KBr) ν: 3409 (OH), 1476, 1439, 1344, 1229, 1182, 1127, 1104 (m), 965 (m), 937 (m), 733 (m), 689 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 26 °C, TMS) δ 2.6 (1H, d, $^2J_{(H,H)} = 7$ Hz, OH), 5.6 (1H, dd, $^2J_{(H,H)} = 9$ Hz and $^2J_{(H,F)} = 23$ Hz, CH), 7.2–7.5 (3H, m, ArH), 7.6–7.7 (2H, m, ArH); ^{19}F NMR (470.5 MHz, $CDCl_3$, CF_3CO_2H) δ −3.1 (3F, s, CF_3), −34.2 (1F, d, $^2J_{(F,F)} = 279$ Hz, CF_2), −45.9 (1F, d, $^2J_{(F,F)} = 279$ Hz, CF_2), −46.7 (1F, d, $^2J_{(F,F)} = 296$ Hz, CF_2), −48.3 (1F, d, $^2J_{(F,F)} = 296$ Hz, CF_2); MS (70 eV): *m*/*z* (%): 355 (20) $[M^+ - 1]$, 149 (100).
6 A. Chieffi, J. V. Comasseto, in *Organoselenium Chemistry*, ed. by T. G. Back, Wiley, New York, **1999**, Chap. 7, p. 145.
7 M. R. Detty, *Tetrahedron Lett.* **1978**, *19*, 5087; D. Liotta, P. B. Paty, J. Johnston, G. Zima, *Tetrahedron Lett.* **1978**, *19*, 5091.
8 D. L. J. Clive, S. M. Menchen, *J. Org. Chem.* **1979**, *44*, 4279.
9 Na: a) D. Liotta, U. Sunay, H. Santiesteban, W. Markiewicz, *J. Org. Chem.* **1981**, *46*, 2605. b) S. V. Ley, I. A. O'Neil, C. M. R. Low, *Tetrahedron* **1986**, *42*, 5363. Li: c) A. B. Smith, III, R. M. Scarborough, Jr., *Tetrahedron Lett.* **1978**, *19*, 1649. d) M. Tiecco, L. Testaferri, M. Tingoli, D. Chianelli, M. Montanucci, *J. Org. Chem.* **1983**, *48*, 4289. e) F. F. Fleming, J. J. Pak, *J. Org. Chem.* **1995**, *60*, 4299.
10 M. Miyashita, M. Hoshino, A. Yoshikoshi, *Tetrahedron Lett.* **1988**, *29*, 347.
11 N. D. P. Cosford, R. F. Schinazi, *J. Org. Chem.* **1991**, *56*, 2161.
12 K. Yokota, M. Taniguchi, T. Kawai, *J. Am. Chem. Soc.* **2007**, *129*, 5818.

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