# Tautomeric Equilibrium between Selenol and Selenoxo Forms of Selenocarboxylic Acids

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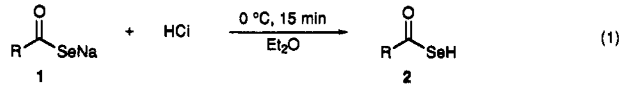
Carboxylic (RCOOH) and thiocarboxylic acids (RCOSH) are ubiquitous but important organic compounds with a great variety of use in chemistry.[1] In contrast, the reactivity and structural features of selenocarboxylic acids (hereafter called selenoic acids) have little been studied mainly because of the lack of their general synthetic methods.[2-4] In the previous synthetic efforts to attain such compounds, the isolation was hampered by the use of strong bases or water and resulted in decomposition.[3] Recently, we have succeeded in the preparation of selenoic acid alkali metal salts, compounds which can be stored under an inert atmosphere.[5] Herein, we report the first isolation of selenoic acids and their behavior in solution indicating the tautomeric equilibrium between selenol and selenoxo forms of selenoic acids.

The preparation of selenoic acids **2** was attained by the treatment of sodium selenocarboxylates **1**[5b] with an ether solution of hydrogen chloride under an Ar atmosphere (eq 1).[6] Table 1 summarizes the yields of **2** and the selected data of their spectroscopic properties. The conversion of **1** to **2** was complete within 15 min. The obtained aliphatic acids **2a–e** are pale yellow liquids, while aromatic acids **2f–l** are pale yellow to red oils or crystalline solids. Some of them could be purified by distillation or recrystallization, which was indicative of the thermal stability of **2**. Although upon exposure to the air compounds **2** were immediately oxidized to the corresponding diselenides, no appreciable change was observed in the solid state at 0 °C for at least 1 month under an Ar atmosphere. In particular, the introduction of the $OCH_3$ group on the aromatic ring highly enhanced the stability of **2j** and **2k**. Characteristic absorptions of the SeH and C=O stretches were observed at 2290–2324 and 1690–1720 cm$^{-1}$, respectively, in the IR spectra. The $^{13}C$ NMR spectra exhibited the signals of the C=O moiety at 190–200 ppm. These data confirmed that selenoic acids existed in the selenol form in the solid state and in a nonpolar solvent similarly to the case of thioic acids.[7]



(1)

Table 1. Yields and Physical Properties of Selenocarboxylic Acids **2** (RCOSeH)

| no. | R | yield$^a$ (%) | IR$^b$ (cm$^{-1}$) $\nu_{SeH}$ | IR$^b$ (cm$^{-1}$) $\nu_{C=O}$ | $^1H$ NMR$^c$ δ SeH | $^{13}C$ NMR$^c$ δ C=O |
|---|---|---|---|---|---|---|
| **2a** | $C_2H_5$ | 88$^d$ | | 1716 | 4.74 | 198.6 |
| **2b** | $i$-$C_3H_7$ | 85$^d$ | 2322 | 1715 | 2.50 | 203.4 |
| **2c** | $t$-$C_4H_9$ | 97$^e$ | 2324 | 1720 | 2.66 | 206.7 |
| **2d** | $n$-$C_5H_{11}$ | 95$^f$ | 2321 | 1715 | 3.70 | 198.5 |
| **2e** | 1-adamantyl | 98$^g$ | 2300$^{h,i}$ | 1719$^{h,i}$ | 2.76$^i$ | 198.5 |
| **2f** | $C_6H_5$ | 91$^j$ | 2320$^k$ | 1694 | 4.48 | 191.7 |
| **2g** | 2-$CH_3C_6H_4$ | 77$^j$ | 2318 | 1694 | 3.57 | 193.4 |
| **2h** | 4-$CH_3C_6H_4$ | 95$^j$ | 2316 | 1692 | 2.37 | 190.9 |
| **2i** | 2-$CH_3OC_6H_4$ | 95$^j$ | 2290 | 1686 | 3.20 | 187.6 |
| **2j** | 4-$CH_3OC_6H_4$ | 96$^l$ | 2289$^h$ | 1682$^h$ | 2.59 | 189.6 |
| **2k** | 2,6-$(CH_3O)_2C_6H_3$ | 77$^m$ | 2296$^h$ | 1682$^h$ | 3.14 | 190.2 |
| **2l** | 1-naphthyl | 92$^j$ | 2314 | 1690 | 3.69 | 193.2 |

[a] Isolated yields. [b] Neat. [c] Chemical shifts are in ppm from internal TMS in $CDCl_3$. [d] The products was a liquid. [e] Bp 68–73 °C/30 Torr. [f] Bp 70–71 °C/17 Torr. [g] Mp 29–30 °C. [h] Nujol. [i] The data for crude **2e** was reported; see ref 3c. [j] The product was an oil. [k] IR absorption for crude **2f** was reported; see ref 3b. [l] Mp 49–50 °C. [m] Mp 63–65 °C.

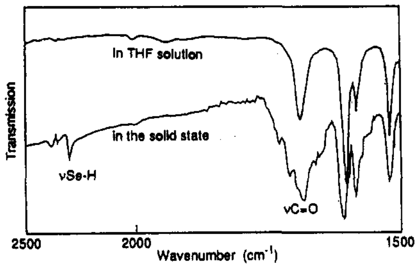


**Figure 1.** Comparison of IR spectra in THF solution and in the solid state for acid **2j**.

When selenoic acids **2** were dissolved in a polar solvent such as $Et_2O$, THF, or MeOH, the color of the solution instantly changed to red, whereas hexane, benzene, and $CHCl_3$ solutions of **2** were light yellow. The IR and NMR spectra of this red solution showed some critical differences from those in Table 1. As shown in Figure 1, the intensity of the C=O stretch of **2j** at 1682 cm$^{-1}$ was reduced in THF as compared with that in the solid state. The signals corresponding to the Se—*H*, *C*=O, and *Se*—H moieties were not detected in $^1H$, $^{13}C$, and $^{77}Se$ NMR spectra. Furthermore, the UV–visible spectrum showed the absorption ascribed to the n–π* transition of the C=Se moiety at 502 nm (Figure 2).[8] These spectra have clearly indicated that the tautomeric equilibrium between selenol form **3** and selenoxo form **4** exists in a polar solvent (eq 2). The $^{13}C$ and $^{77}Se$ NMR spectra at −90 °C exhibited the signals only due to carbon and selenium

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[1] (a) Falbe, J., Ed. *Houben-Weyl Methoden der Organischen Chemie*; Georg Thieme Verlag: Stuttgart, 1985; p E5. (b) Knight, D. W. *Gen. Synth. Methods* **1992**, *13*, 79. (c) Patai, S., Ed. *Supplement B: The Chemistry of Acid Derivatives*; John Wiley & Sons: New York, 1992; Vols. 1, 2.

[2] (a) Jensen, K. In *Organic Selenium Compounds: Their Chemistry and Biology*; Klayman, D. L.; Günther, W. H. H., Eds.; Wiley-Interscience: New York, 1973; pp 263–272. (b) Guziec, F. S., Jr. In *The Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S., Ed.; John Wiley & Sons: New York, 1987; Vol. 2, pp 215–273. (c) Guziec, F. S., Jr. In *Organoselenium Chemistry*; Liotta, D., Ed.; Wiley-Interscience: New York, 1987; p 277.

[3] (a) Jensen, K. A.; Bøje, L.; Henriksen, L. *Acta Chem. Scand.* **1970**, *24*, 3213. (b) Ishihara, H.; Kato, S. *Tetrahedron Lett.* **1972**, 3751. (c) Hirabyashi, Y.; Ishihara, H.; Echigo, M. *Nippon Kagaku Kaishi* **1987**, 1430.

[4] On the contrary, selenoic acid esters have recently provided fruitful chemistry: Ogawa, A.; Sonoda, N. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 6, p 461.

[5] (a) RCOSeLi: Kojima, Y.; Ibi, K.; Kanda, T.; Ishihara, H.; Murai, T.; Kato, S. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 990. (b) RCOSeNa: Kato, S.; Kageyama, H.; Takagi, K.; Mizoguchi, K.; Murai, T. *J. Prakt. Chem.* **1990**, *332*, 897. (c) RCOSeK: Kageyama, H.; Takagi, K.; Murai, T.; Kato, S. *Z. Naturforsch.* **1989**, *44b*, 1519. (d) RCOSeRb, RCOSeCs: Kawahara, Y.; Kato, S.; Kanda, T.; Murai, T.; Ishihara, H. *J. Chem. Soc., Chem. Commun.* **1993**, 277.

[6] A typical experimental procedure is as follows: A solution of dry hydrogen chloride (2.0 mmol)/ether (2.0 mL) was added to a suspension of sodium 4-methoxybenzenecarboselenoate (**1j**) (0.739 g, 2.5 mmol) in the same solvent (25 mL), and the mixture was stirred at 0 °C for 15 min. Removal of the precipitates (NaCl and excess **1j**) by filtration, evaporation of the ether under reduced pressure, and recrystallization of the resulting residue (orange solid) from hexane yielded 516 mg (96%) of 4-methoxybenzenecarboselenoic acid (**2j**) as yellow microcrystals. **2j**: mp 49–50 °C; IR (Nujol, cm$^{-1}$) 3050, 2972, 2877, 2289 ($\nu_{SeH}$), 1682 ($\nu_{C=O}$), 1600, 1574, 1508, 1464, 1419, 1378, 1306, 1264, 1215, 1167, 1114, 1020, 895, 840, 649, 615, 450; $^1H$ NMR ($CDCl_3$) δ 2.59 (brs, 1H, SeH), 3.86 (s, 3H, $CH_3O$), 6.92 (d, $J$ = 8.8 Hz, 2H, Ar), 7.82 (d, $J$ = 8.8 Hz, 2H, Ar); $^{13}C$ NMR ($CDCl_3$) δ 55.6 ($OCH_3$), 114.0, 130.3, 131.0, 164.3 (Ar), 189.6 (C=O); $^{77}Se$ NMR ($CDCl_3$) δ 427.5; HRMS calcd for $C_8H_9O_2Se$ 215.968 92, found 215.969 90. Anal. Calcd for $C_8H_8O_2Se$: C, 44.67; H, 3.75. Found: C, 44.95; H, 3.72.

[7] Scheithauer, S.; Mayer, R. In *Topics in Sulfur Chemistry*; Senning, A., Ed.; Georg Thieme Publishers: Stuttgart, 1979; Vol. 4. See also ref 1a.

[8] The n–π* transitions of the known compounds having the C=Se moiety are as follows: 4-$CH_3OC_6H_4CSeOSiMe_3$, 527 nm (log ε 2.08);[9] $C_6H_5CSe$-$OPr$-$i$, 504 nm (log ε 2.11).[10]

[9] Kato, S.; Kageyama, H.; Kawahara, Y.; Murai, T.; Ishihara, H. *Chem. Ber.* **1992**, *125*, 417.

[10] Barton, D. H. R.; Hansen, P.-E.; Picker, K. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1723.

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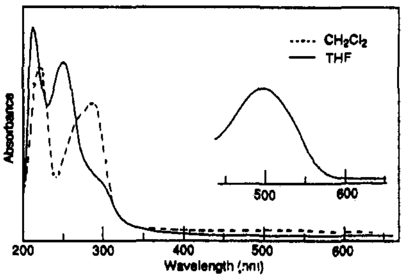

**Figure 2.** Absorption spectra recorded in $CH_2Cl_2$ solution and in THF solution for acid **2j**.

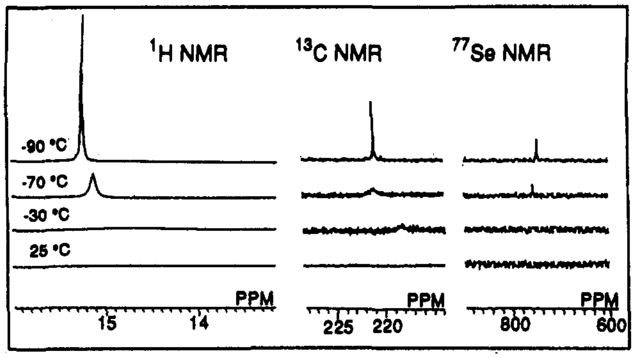

**Figure 3.** Variable low-temperature NMR spectra in $d_8$-THF solution for acid **2j**.

(2)

**3** **4**

of the C=Se moiety at 222.2 and 753.9 ppm, respectively.[11] The existence of hydrogen-bonding interactions with THF was also detected by the signal at 15.3 ppm in the $^1$H NMR spectrum. These sharp signals were broadened substantially upon raising the temperature (Figure 3). *This apparently suggests that the selenoxo form **4** is a dominating species at low temperature in THF.* Encouraged by these results, similar spectroscopic measurements were carried out with the better known thioic acids. Interestingly, despite the previous understanding that a thiol form predominated over a thioxo form,[12] the thioxo form was found to be the only species observed for $4\text{-}CH_3OC_6H_4COSH$ in a polar solvent. Thioamides and selenoamides also have heteroatom-stabilized carbon–chalcogen double bonds and can exist formally in two tautomeric forms. The molecular orbital calculations concerning these molecules have suggested that the imido form becomes stable in going from thioamides to selenoamides.[13] Nevertheless, the selenoic acids can exist exclusively in the selenoxo form at low temperature in spite of the fact that they require double bonding between carbon and selenium, which is more energetically unfavorable than that between carbon and sulfur.[14] In a polar solvent, hydrogen-bonding interactions of **3** with the solvent may allow for the electrons on the selenocarboxyl group to delocalize more easily. In the system at low temperature, the equilibrium in eq 2 is shifted to **4**. This may be understood by considering the notion that the proton on the selenocarboxyl group localizes on the more electronegative atom, i.e., oxygen rather than selenium, and this enables the involvement of the C=Se bond in **4**.

The high reactivity of selenoic acids was confirmed by the reaction with dicyclohexylcarbodiimide (DCC).[15] The addition of selenoic acids to DCC was complete within 1 h to give quantitatively the corresponding diacyl selenides and selenourea. Accordingly, the selenoic acids are at least as reactive as thioic[16] and dithioic acids.[17]

In summary, we have demonstrated the first successful isolation of selenoic acids **2** prepared from **1**. The existence of the tautomeric equilibrium between selenol and selenoxo forms was spectroscopically proved for the first time. The selenoxo form is not a canonical form but an actual species in a polar solvent at low temperature regardless of the involvement of the C=Se bond, whereas **2** exists dominantly in the selenol form in the solid state and in a nonpolar solvent. The present system is an example of heteroatom-containing allylic anion systems and suggests that electronegativity and hydrogen-bonding interaction may play an important role in controlling the degree of the localization of the electron and in forming double bonding even between carbon and a fourth-row element. The equilibrium, acidity, and reactivity results might be of importance not only in designing synthetic applications of selenoic acids but also in understanding the role of Se in biological systems.

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**Supplementary Material Available:** Listings of spectral and analytical data for products **2a–i**, **2k**, and **2l** and the procedure for the acidity test (3 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(11) The assignment of these signals is based on the following $^{13}$C and $^{77}$Se NMR spectral data. $4\text{-}CH_3OC_6H_4CSeOSiMe_3$:[9] *C*=Se, δ 220.6 ($CDCl_3$), 221.3 ($d_8$-THF), C=*Se*, δ 936 ($CDCl_3$). $4\text{-}CH_3OC_6H_4COSeH$: *Se*-H, δ 427.5 ($CDCl_3$).

(12) Randhawa, H. S.; Meese, C. O.; Walter, W. *J. Mol. Struct.* **1977**, *36*, 25.

(13) Leszczynski, J.; Kwiatkowski, J. S.; Leszczynska, D. *J. Am. Chem. Soc.* **1992**, *114*, 10089.

(14) The synthesis and characterization of carbon chalcogen multiple bonds are of current research interest. For reviews, see: (a) Kato, S.; Murai, T.; Ishida, M. *Org. Prep. Proced. Int.*, **1986**, *18*, 369. (b) Okazaki, R. *J. Synth. Org. Chem., Jpn.* **1988**, *46*, 1149. (c) Usov, V. A.; Timokhina, L. V.; Voronkov, M. G. *Sulfur Rep.* **1992**, *12*, 95–158. See also refs 2b,c.

(15) The acidity of selenoic acids was also estimated by mixing them with thioic acid ammonium salts. The preliminary results indicate that selenoic acids may be more acidic than the corresponding thioic acids, see supplementary material.

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(17) Kato, S.; Shibahashi, T.; Katada, T.; Takagi, T.; Noda, I.; Mizuta, M.; Goto, M. *Liebigs Ann. Chem.* **1982**, 1229.