Intramolecular non-bonded interaction between selenium and oxygen as revealed by ^{17}O and ^{77}Se NMR spectroscopy and natural bond orbital analysis

Hiroto Komatsu, Michio Iwaoka and Shuji Tomoda*

Departement of Life Sciences, Graduate School of Arts and Sciences, The University of Tokyo, Komaba, Meguro-ku, Tokyo 153-8902, Japan. E-mail: tomoda@selen.c.u-tokyo.ac.jp

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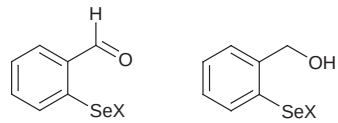
^{17}O and ^{77}Se NMR spectroscopic measurement and natural bond orbital (NBO) analysis of 2-formyl- and 2-hydroxymethyl-benzeneselenenyl derivatives (ArSeX; X = Cl, Br, CN, SPh, SeAr, Me: Ar = C_6H_4CHO, $C_6H_4CH_2OH$) provided strong evidence for the intramolecular non-bonded interaction between selenium and oxygen due to orbital interaction between the oxygen lone pair and the low-lying σ^*_{SeX} antibonding orbital ($n_O \rightarrow \sigma^*_{SeX}$).

Non-bonded interactions involving selenium are an important factor that often dictates the structure and reactivity of organoselenium compounds, some of which are known to be useful for asymmetric synthesis[1] as well as for enzyme-mimetic catalytic reactions.[2] We have recently studied the non-bonded interaction between selenium and nitrogen (Se···N)[3] and selenium and fluorine (Se···F)[4] to characterize the mechanism of the interactions. While the former interaction is stabilized chiefly *via* orbital interaction (donor–acceptor interaction),[3] the stabilization mechanism of the latter may be slightly more electrostatic in nature.[4] From the viewpoint of electronegativity scale,[5] it is expected that the interaction between selenium and oxygen (Se···O) may be intermediate. However the results of the recent publications on the mechanism of Se···O interactions are variable to leave the interaction mechanism of Se···O uncertain.[6]

Herein we report the first systematic NMR study of Se···O interactions. The conclusions drawn from the present NMR study have been corroborated by *ab initio* molecular orbital calculations combined with natural bond orbital (NBO) analysis proposed by Weinhold.[7]

Model compounds, ^{17}O-enriched 2-formylbenzeneselenenyl derivatives (**1a–f**) and 2-(hydroxymethyl)benzeneselenenyl derivatives (**2a–f**), were synthesized from the corresponding



1 **2**

a: X = Cl
b: X = Br
c: X = CN
d: X = SPh (**d'**: X = SMe)
e: X = SeAr (**e'**: X = SeMe)
f : X = Me

^{17}O-enriched diselenide (**1e**) according to literature methods.[8] These compounds were obtained in spectrally pure form except for **1d** and **2d**, which slowly disproportionated into the corresponding diselenides (**1e** and **2e**) at room temperature.

Since ^{17}O nuclear spin is a quadrupole, attempts at observing the one-bond spin–spin coupling constant between the non-bonded ^{17}O and ^{77}Se ($^1J_{Se\cdots O}$), which was thought to provide direct information as to the intramolecular non-bonded interaction between these nuclei, was unsuccessful. The ^{17}O NMR chemical shift data (δ_O) for compounds **1** and **2**, obtained at 67.70 MHz, are collected in Table 1 along with those of ^{77}Se NMR chemical shift (δ_{Se}), measured at 95.35 MHz. Three notable features are seen from Table 1.

First, within the series of compounds **1**, a monotonous downfield shift of δ_O is observed on going from **1a** to **1f** (δ_O = 493.0 → 561.6), while exactly the opposite trend is apparent for δ_O for **2** (δ_O = 24.9 → 10.6). Secondly, δ_O values for **1** (δ_O = 493.0–561.6), each of which possesses an sp^2-hybridized oxygen, are shifted toward upfield ($\Delta\delta_O$ = −76 to −7) compared with that of a reference benzaldehyde, which lacks the selenium moiety (δ_O = 569),[9] whereas δ_O values for **2** (δ_O = 24.9–10.6), each of which bears an sp^3-hybridized oxygen, are shifted downfield ($\Delta\delta_O$ = 24.2–9.9) compared to that of reference compound benzyl alcohol (δ_O = 0.7).[10] The mutually inverse effect on the relative chemical shift ($\Delta\delta_O$) precludes the possibility of major inductive through-bond electronic effects of the selenium moiety (SeX). These experimental data strongly suggest that a Se···O interaction (attractive or repulsive) may exist at least in one of these compound series. It should be noted that the absolute magnitude of these shifts ($\Delta\delta_O$) steadily decrease on going from **a** through **f** for both series. Thirdly, comparison of ^{77}Se chemical shifts (δ_{Se}) between compounds **1** and **2** possessing the same substituent X reveals that the former (1114.1–259.5) is considerably lower than the latter (987.1–157.2), clearly suggesting that there should be a stronger Se···O interaction in series**1** than in **2** ($\Delta\delta_{Se}$ = 25.3–190.0): the significant downfield shift may be caused on the selenium nucleus by the anisotropic deshielding effect of the formyl C=O bond of **1** if the selenium lies coplanar with the C=O bond.

It is well known[11] that a linear dependence of ^{17}O NMR chemical shift on the amount of electronic charge on the oxygen atom generally exists within a series of structurally similar compounds: for an sp^2-hybridized oxygen atom, the higher the charge, the larger the magnitude of upfield shift of ^{17}O NMR chemical shift, while exactly the opposite trend is observed for sp^3-hybridized oxygen. According to this rule, the dependence of the chemical shift (δ_O) on substituent X seen from Table 1 suggests that for both series of compounds (**1** and **2**) the electronic charge on the oxygen atom in the conformation with

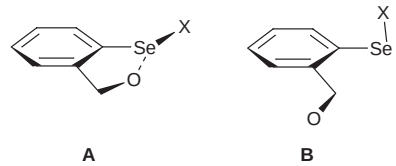
Table 1 ^{17}O and ^{77}Se NMR chemical shifts (δ_O and δ_{Se}) of **1** and **2**[a]

		1			**2**			
	X	δ_O[b]	$\Delta\delta_O$[c]	δ_{Se}[d]	δ_O[b]	$\Delta\delta_O$[e]	δ_{Se}[d]	$\Delta\delta_{Se}$[f]
a	Cl	493.0	−76	1114.1	24.9	+24.2	987.1	127.0
b	Br	515.9	−53	1029.5	23.2	+22.5	839.5	190.0
c	CN	548.0	−21	426.7	22.0	+21.3	314.5	111.8
d	SPh	556.6	−12	621.7	16.0	+15.3	501.8	119.9
e	SeAr	559.3	−10	458.5	13.3	+12.6	433.2	25.3
f	Me	561.6	−7	259.5	10.6	+9.9	157.2	102.3

[a] Measured in $CDCl_3$ at 298 K. [b] Measured at 67.70 MHz with D_2O as an external standard. [c] Relative ^{17}O NMR chemical shift with respect to PhCHO (δ_O = 569).[9] [d] Measured at 95.35 MHz with Me_2Se as an external standard. [e] Relative ^{17}O NMR chemical shift with respect to $PhCH_2OH$ in acetone (δ_O = 0.7).[10] [f] $\Delta\delta_{Se} = \delta_{Se}(\mathbf{1}) - \delta_{Se}(\mathbf{2})$.

Se···O interaction should decrease monotonously on going from **a** to **f**.

Strong theoretical evidence for the existence of attractive Se···O interaction as well as for the definitive trend of the electronic charge at oxygen atom for both series of compounds has been obtained with *ab initio* molecular orbital calculations[12] and natural bond orbital (NBO) analysis.[7] See http://www.rsc.org/suppdata/cc/1999/205 for summary of results as electronic supplementary information. Initial conformational search of **1** and **2** at the RHF/3-21G* level indicated two stable conformational isomers for both series of model compounds (Scheme 1). Conformer **A**, in which the O–Se–X angle is nearly 180°, has a close Se···O contact, whereas conformer **B**, in which the Se–X bond is almost perpendicular to the plane of the phenyl ring, does not. For all model compounds calculated with 6-31G(d,p) basis for C, H, N, O, S, and Cl and Huzinaga's 43321/4321/311(d) basis set for Se and for Br,[13] conformer **A** was found to be more stable by ΔE_{tot} = 0.44–9.99 kcal mol^{-1}, strongly suggesting that the Se···O interaction may be attractive in all cases in consonant with the trends manifested by the ^{17}O and ^{77}Se NMR chemical shift data.



Scheme 1

Natural population analysis (NPA) of these conformers indicates the following three intriguing points with regard to the electron population at oxygen atom in conformers **A** and **B** (q_A and q_B). First, the populations at the oxygen atom of **2** (*ca.* −0.8 e) are uniformly greater than those of **1** (*ca.* −0.6 e) irrespective of substituent X. Secondly, relative oxygen populations with respect to the reference compounds (PhCHO for **1** and $PhCH_2OH$ for **2**) for conformer **A** (Δq_A) are negative, indicating that Se···O interaction might induce a small increment of electron density at the oxygen and that this is larger in **1** (Δq_A = 0.000 to −0.025) than in **2** (Δq_A = −0.001 to −0.008). Thirdly, such a tendency is attenuated on going from **a** to **f** for both series, which may imply that the magnitude of the Se···O interaction is diminished in this order. In full agreement with the previous observation[11] on the linear relationship between the charge at oxygen and ^{17}O NMR chemical shift, Δq_A indeed exhibits a linear correlation with $\Delta\delta_O$ (r^2 = 0.89 and 0.90 for series **1** and **2**, respectively), indicating that conformer **A** is more stable for both series **1** and **2**.

NBO deletion analysis, which is known to be an effective method of quantitative evaluation of attractive orbital interaction alone,[7] has been applied to conformer **A** for both compound series to estimate the strength of the Se···O interaction due to orbital interaction mechanism (E_{del}). Series **1** has E_{del} = 16.6–6.1 kcal mol^{-1} and **2** has E_{del} = 6.8–1.9 kcal mol^{-1}. A remarkable linear correlation was observed between the Se···O distance ($d_{Se\cdots O}$) and the NBO deletion energy (E_{del}) for each series (r^2 = 0.98 for **1** and 0.96 for **2**), which may suggest that the attractive Se···O interaction should arise chiefly from orbital interaction. NBO second-order perturbation analysis indicated that the major orbital interaction is that between the oxygen lone pair (n_O) and the low-lying σ^*_{SeX} antibonding orbital ($n_O \rightarrow \sigma^*_{SeX}$). It is apparent that this interaction energy explains most of E_{del} in all cases. Interestingly an excellent linear correlation was observed between the relative chemical shift ($\Delta\delta_O$) and E_{del} for each series of model compounds. For series **1**, the slope of the correlation is negative (r^2 = 0.96), whereas for **2** it is positive (r^2 = 0.90), indicating that both upfield shift for series **1** and downfield shift for series **2** should be roughly proportional to the magnitude of the Se···O interaction due to orbital interaction mechanism (E_{del}). It is particularly noteworthy that highly electronegative substituent (X), such as CN, shows almost no deviation from linearity, which may preclude the possibility of electrostatic mechanism of Se···O interaction in these compounds.

In summary, the linear correlations among the three parameters for conformer **A** of both series **1** and **2** namely, $\Delta\delta_O$, E_{del} and Δq_A, are in full accord with the existence of attractive non-bonded Se···O interactions, the major mechanism of which is most likely to be the orbital interaction between the oxygen lone pair (n_O) and the low-lying σ^*_{SeX} antibonding orbital. Possible enhanced strength of the attractive Se···O interaction in **1** *cf.* **2** may be most simply explained in terms of π-conjugation between the formyl group and the phenyl ring in **1**, which may encumber free rotation around the C(Ph)–CH bond to generate a stable conformation of **1** with a Se···O distance that is shorter ($d_{Se\cdots O}$ = 2.58–2.86 Å) than those of **2** ($d_{Se\cdots O}$ = 2.82–3.17 Å).

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