How Selenium's Electronic Structure Favor Its Participation in Non-covalent Interactions?

Ass. Prof. Dr. Elena Yu. Tupikina,
Valeria V. Mulloyarova,
Danil V. Krutin,
Anton S. Zakharov,
Peter M. Tolstoy
St. Petersburg University,
Russia
elenatupikina@gmail.com

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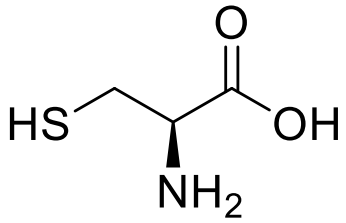
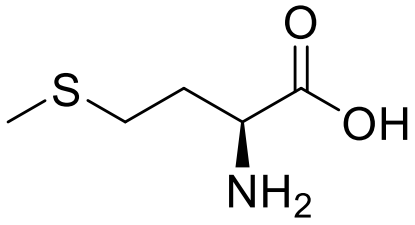
- **Part I. Polarizability of selenium electronic shell**
- Part II. Se···Se short contacts
- Part III. $R_3P{=}Se$ – NMR spectral probes for NCIs investigation

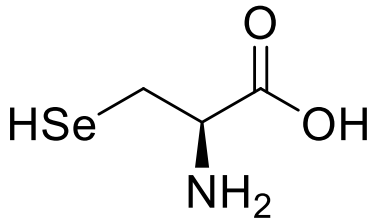
Sulphur- vs selenium-containing amino acids



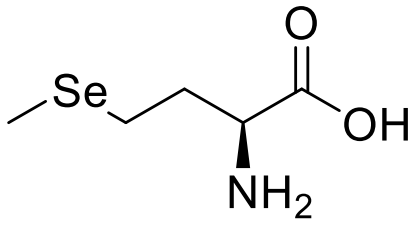
cysteine



methionine



selenocysteine

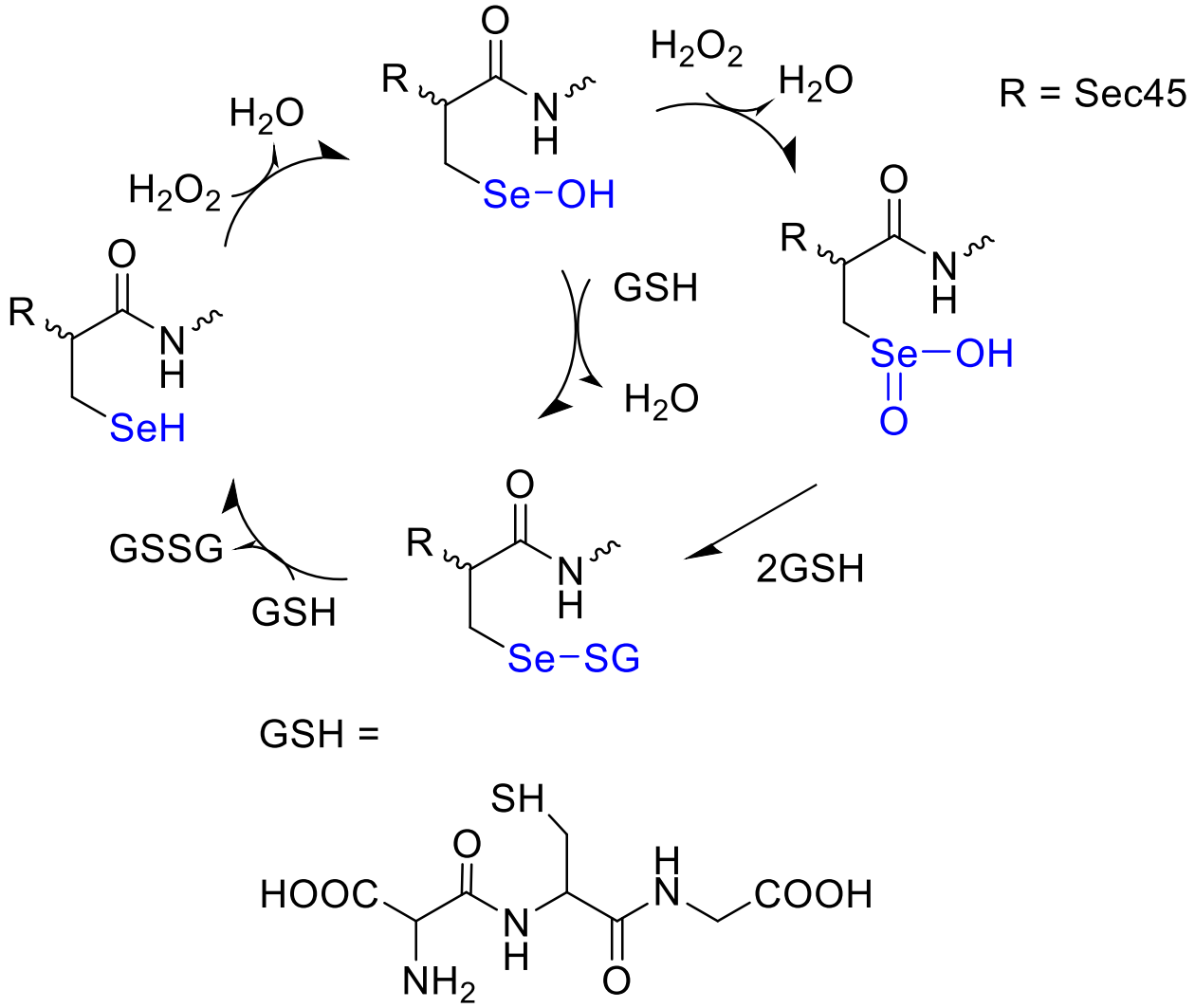


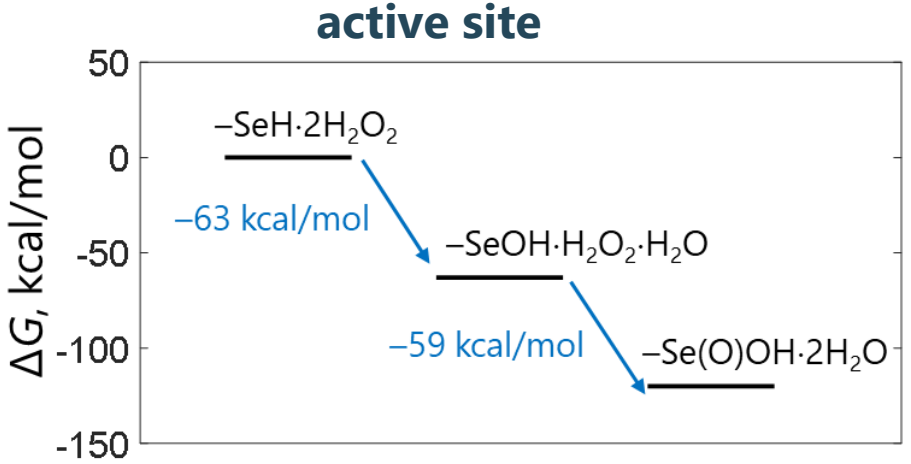
selenomethionine

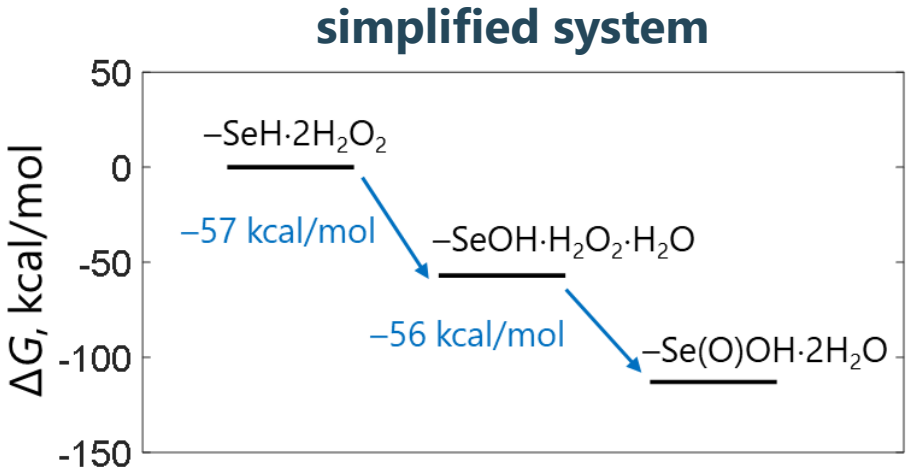
- replacement of a single atom dramatically changes chemical properties

Reich H. J., Hondal R. J. *ACS Chemical Biology* 2016.

The mechanism of peroxide reduction by the GPx-1 enzyme



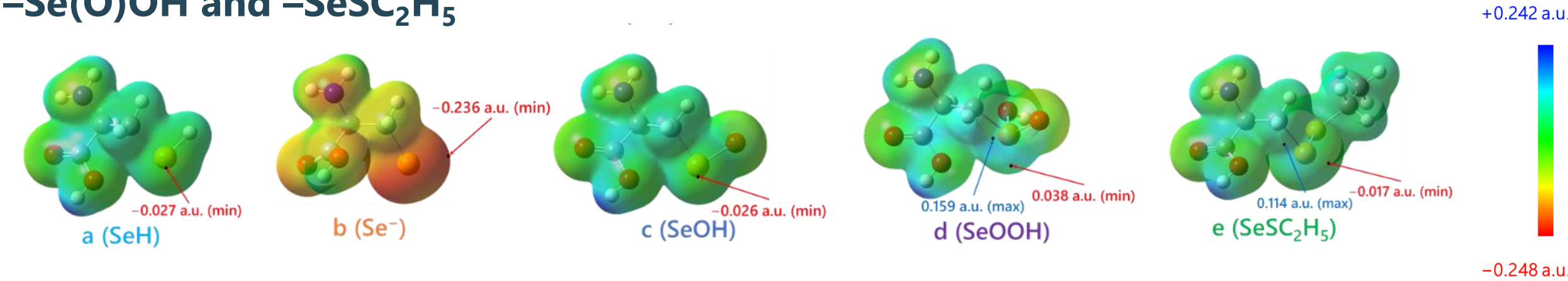


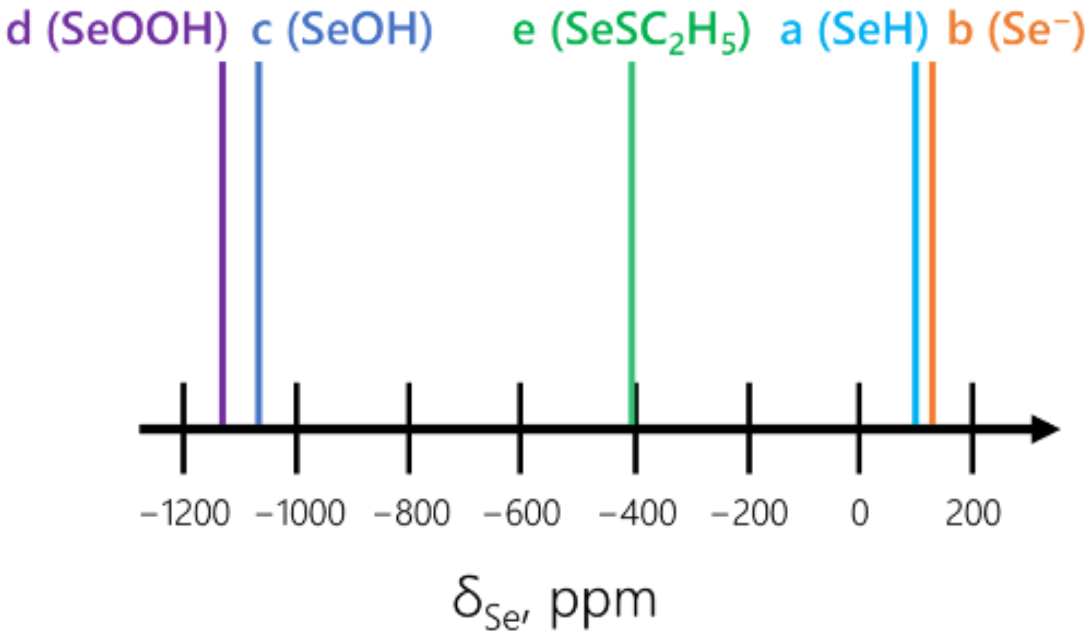


- NCIs with participation of Sec45 increase gain in Δ*G*

Bhowmick, D., Mugesh, G., *Organic & Biomolecular Chemistry* **2015**
Tupikina, E. Yu., *Organic & Biomolecular Chemistry* **2022**

Differences in charge distribution near selenium in case of –SeH, –Se(–), –SeOH, –Se(O)OH and –$SeSC_2H_5$

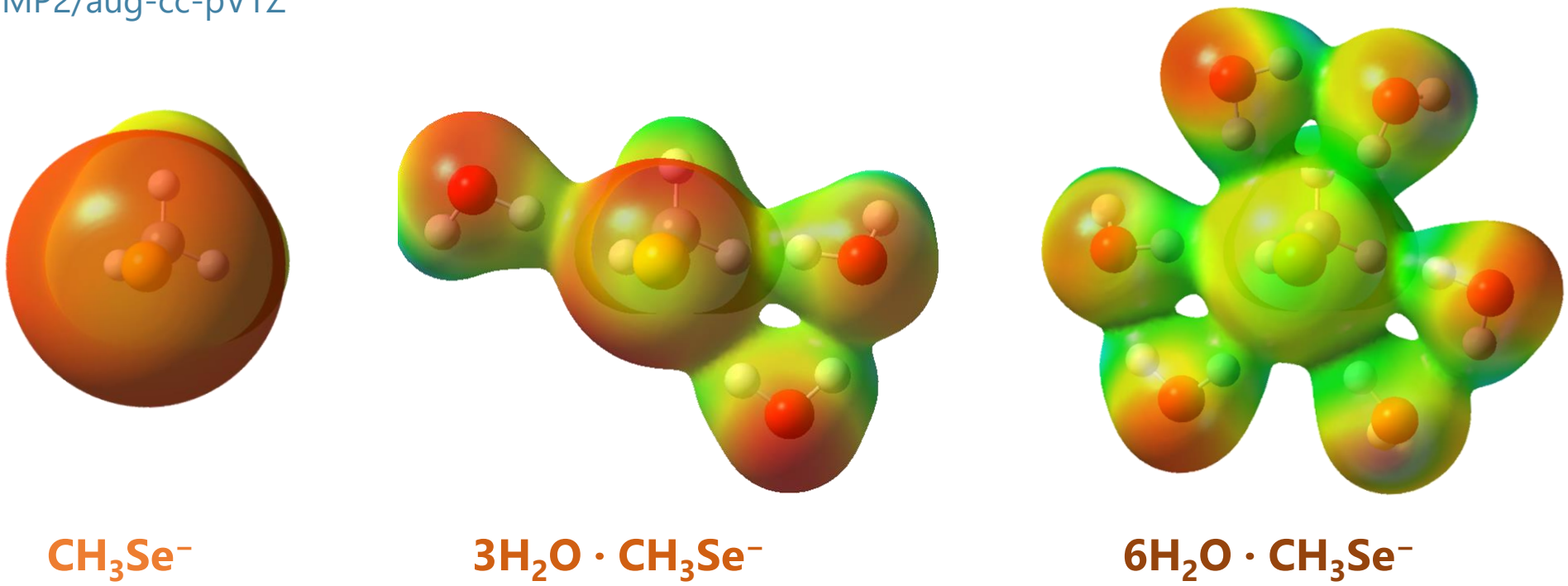




- the number and type of covalent bonds of Se strongly influence its electronic shell

Hydrogen bonds with water molecules in the first coordination sphere of the selenium for CH_3–Se(–): influence on the σ-hole

MP2/aug-cc-pVTZ



CH_3Se^- $3H_2O \cdot CH_3Se^-$ $6H_2O \cdot CH_3Se^-$

–0.226 a.u. **+0.010 a.u.**

- formation of HBs with water changes σ-hole depth

Tupikina, E.Yu. et al. *Phys. Chem. Chem. Phys.* **2021**
Karpov, V.V. et al. *J. Comput. Chem.* **2021**

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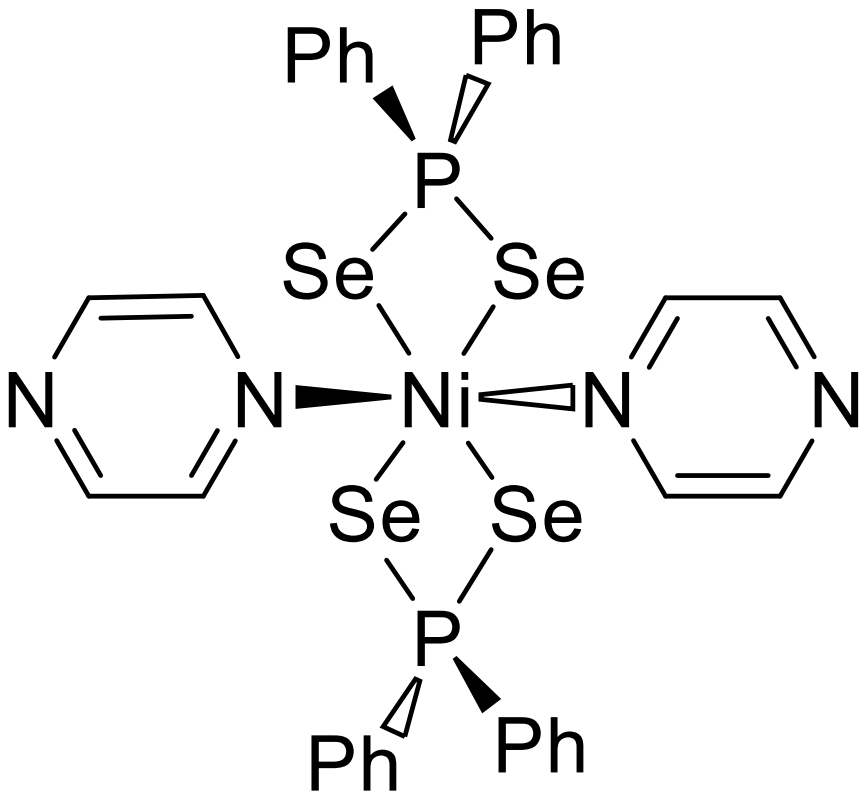
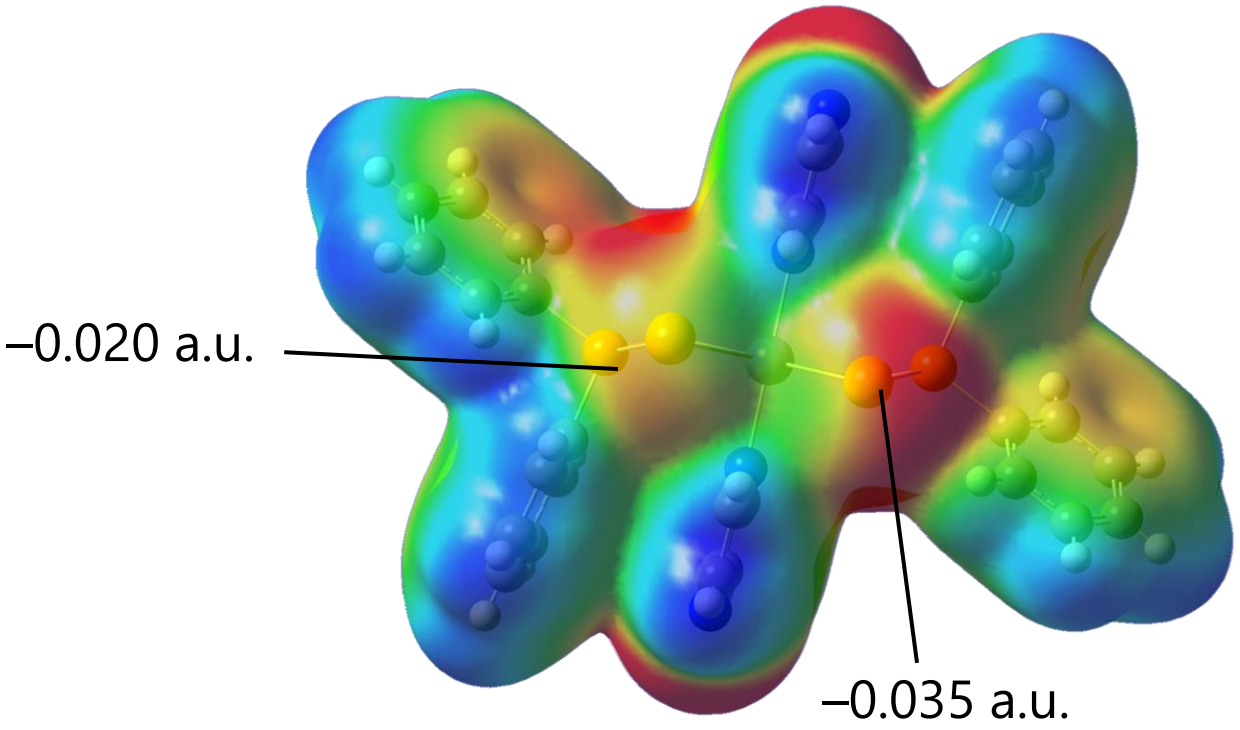
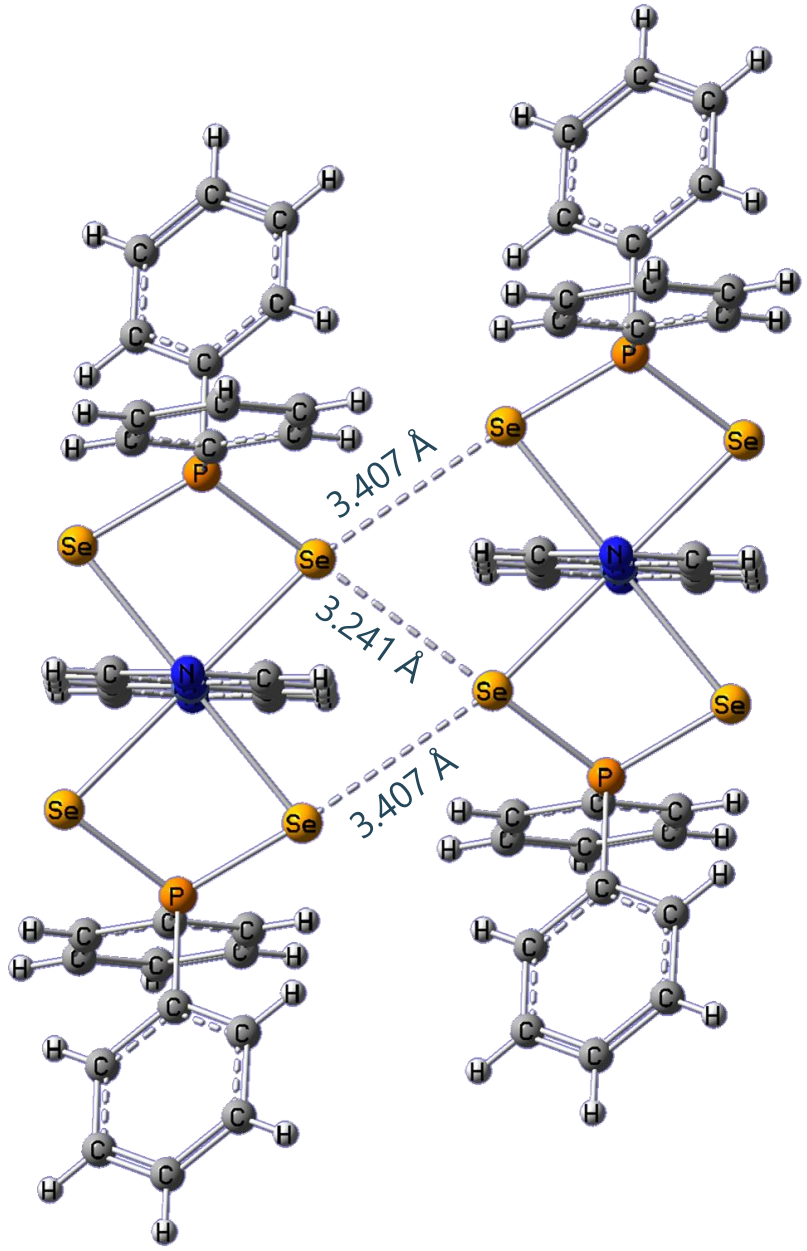
Se···Se interaction



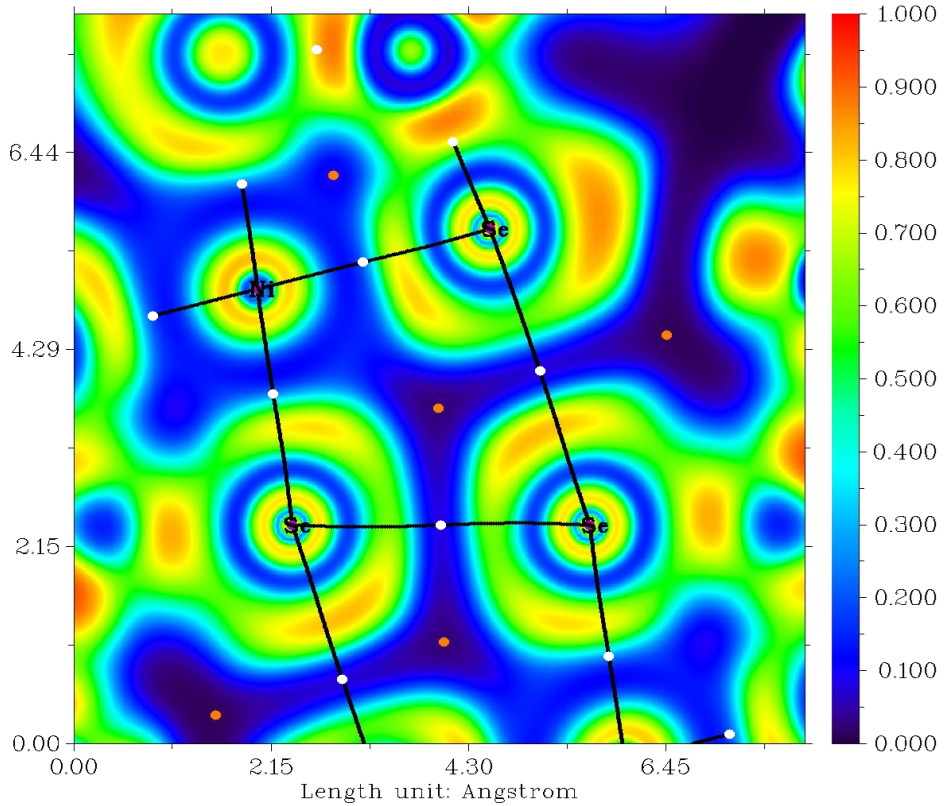


In collaboration with Alexander Artem'ev, Nikolaev Institute of Inorganic Chemistry (RAS)

Se···Se interaction



$r_{Se\cdots Se}$, Å	ρ, a.u.	$\nabla^2\rho$, a.u.	G, a.u.	V, a.u.	H, a.u.
3.407	0.0128	0.0314	0.0070	–0.0061	0.0009
3.241	0.0150	0.0390	0.0089	–0.0080	0.0009



- hole-to-hole Se···Se interaction?!

- Part I. Polarizability of selenium electronic shell
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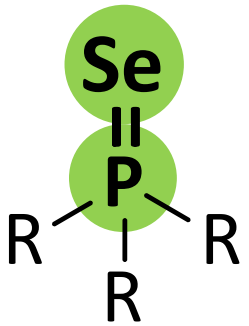
Phosphine selenides – probes for NMR spectral diagnostics of NCIs

Problem

Search for probe molecules capable to participate in **different** NCIs, whose NMR parameters are sensitive to parameters of formed NCIs.

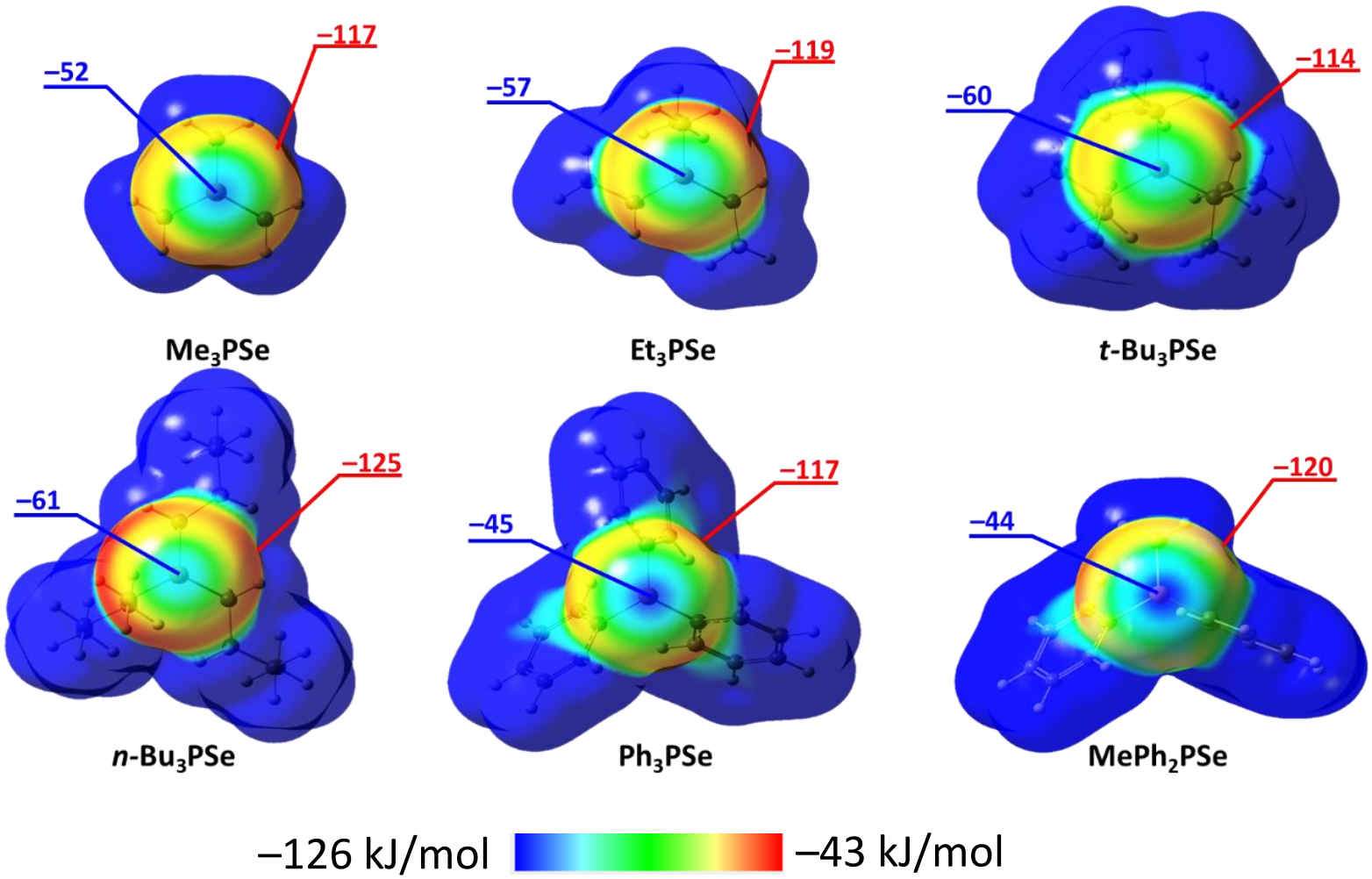
Solution

Use phosphine selenides $R_3P{=}Se$ (R = Me, Et, *t*-Bu, *n*-Bu, Ph)



nucleus	S	ω, %	$\gamma \cdot 10^7$, rad·s^{-1}·T^{-1}
^{31}P	1/2	100	10.8
^{77}Se	1/2	7.6	5.1

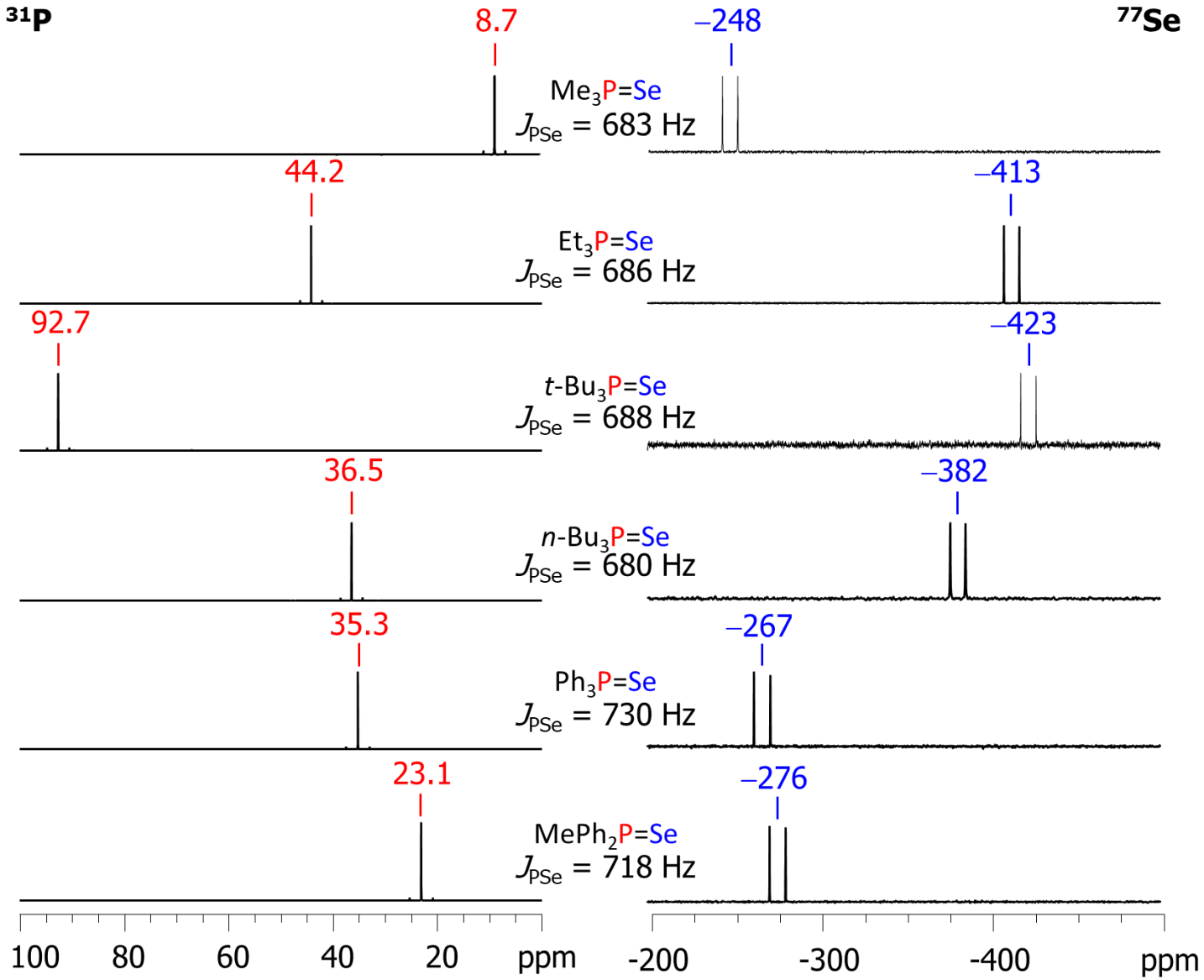
Phosphine selenides – probes for NMR spectral diagnostics of NCIs



- anisotropy of ESP distribution near Se atom make $R_3P{=}Se$ able to participate in NCIs both as electron donor and as electron acceptor

PW6B95-D3/def2-QZVP

Phosphine selenides – probes for NCI spectral diagnostics



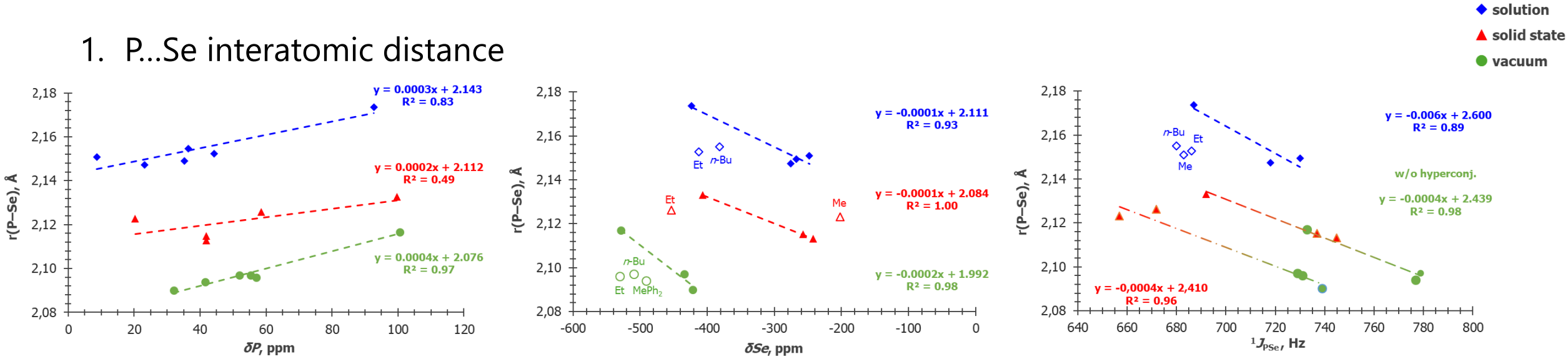
$CDCl_3$, 298 K

- significant variation in δP, δSe and $^1J_{PSe}$ upon change of R

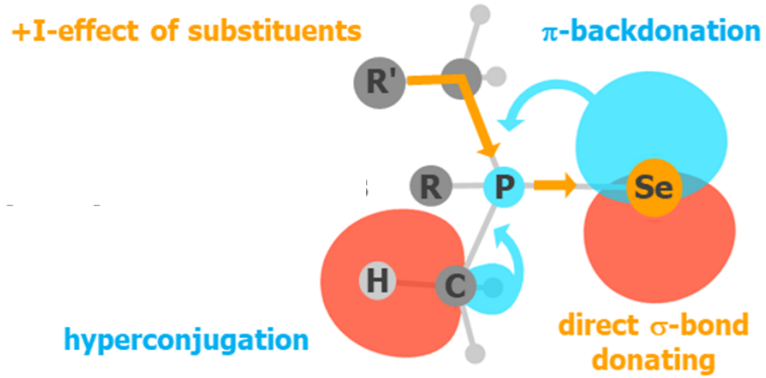
Krutin, D.V., *Phys. Chem. Chem. Phys.* (*under review*)

Factors influencing ^{31}P, ^{77}Se NMR parameters of $R_3P{=}Se$: δP, δSe, $^1J_{PSe}$

1. P…Se interatomic distance



2. Electronic effects



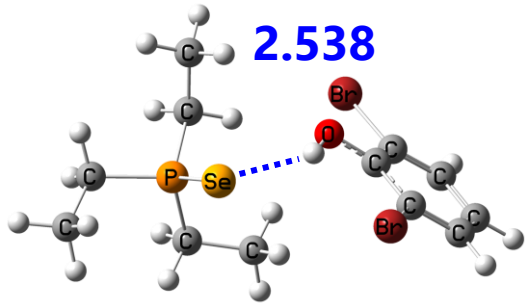
3. Symmetry of selenium atom environment

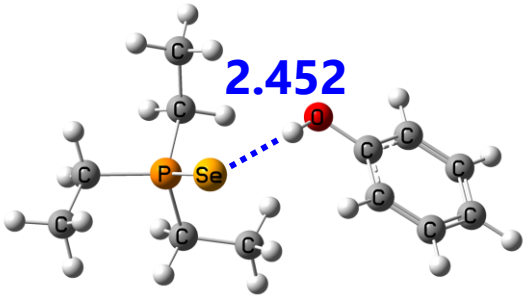
Krutin, D.V., *Phys. Chem. Chem. Phys*. (*under review*)

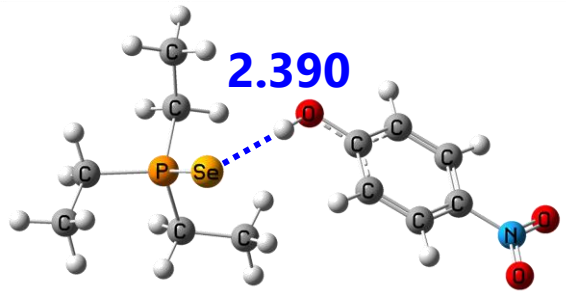
Phosphine selenides – probes for HBs

$Et_3P{=}Se \cdots HO$–(R-substituted phenyl)

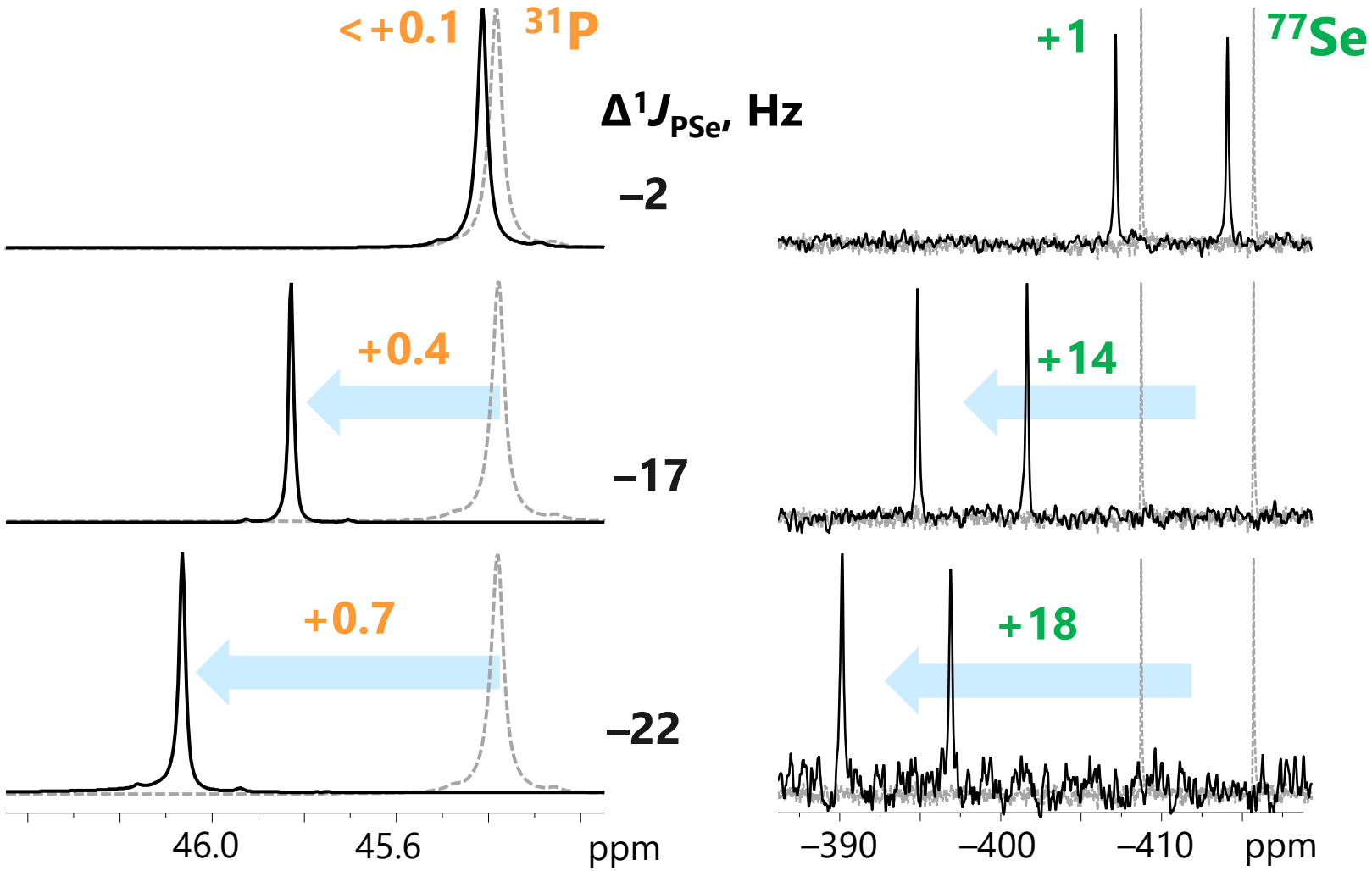
PW6B95-D3/def2-QZVP







$R_{Se\cdots H}$

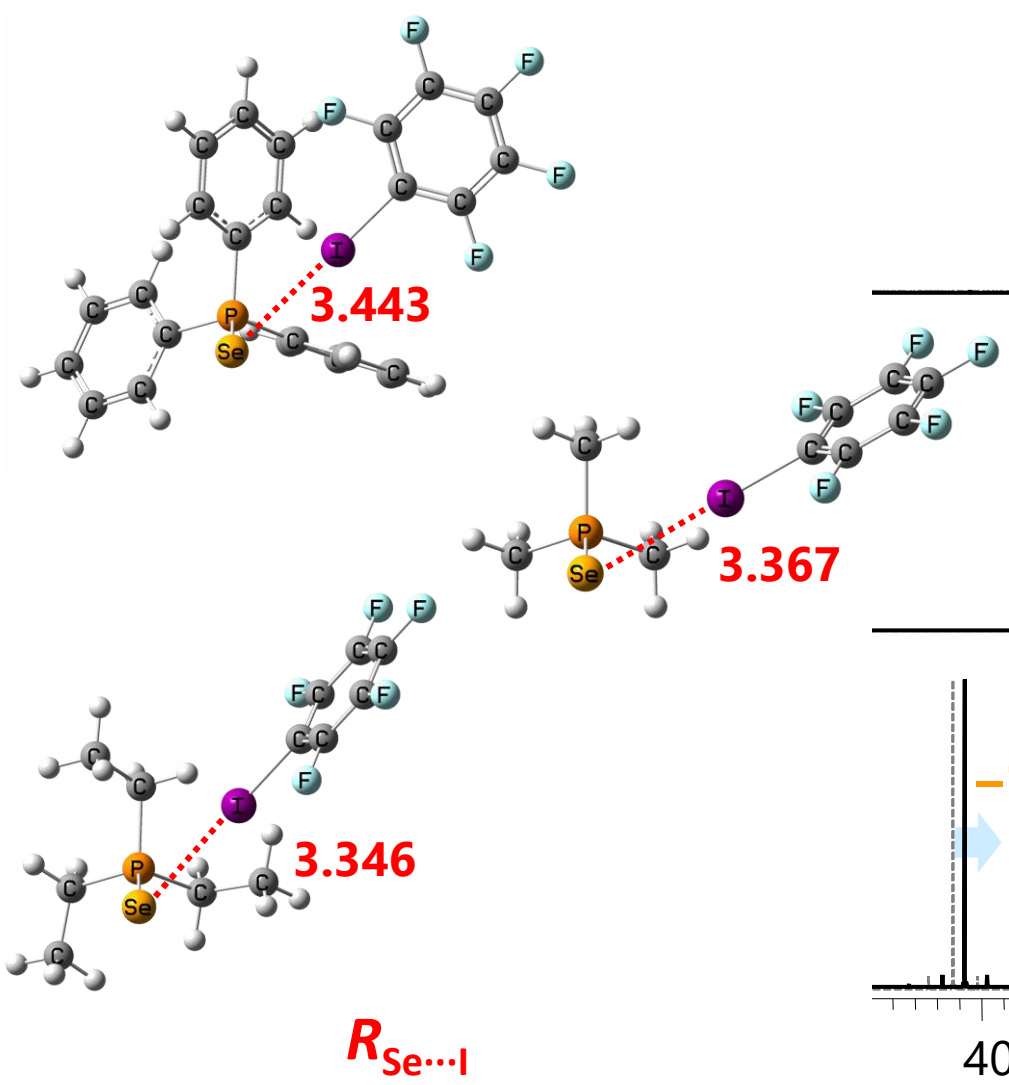


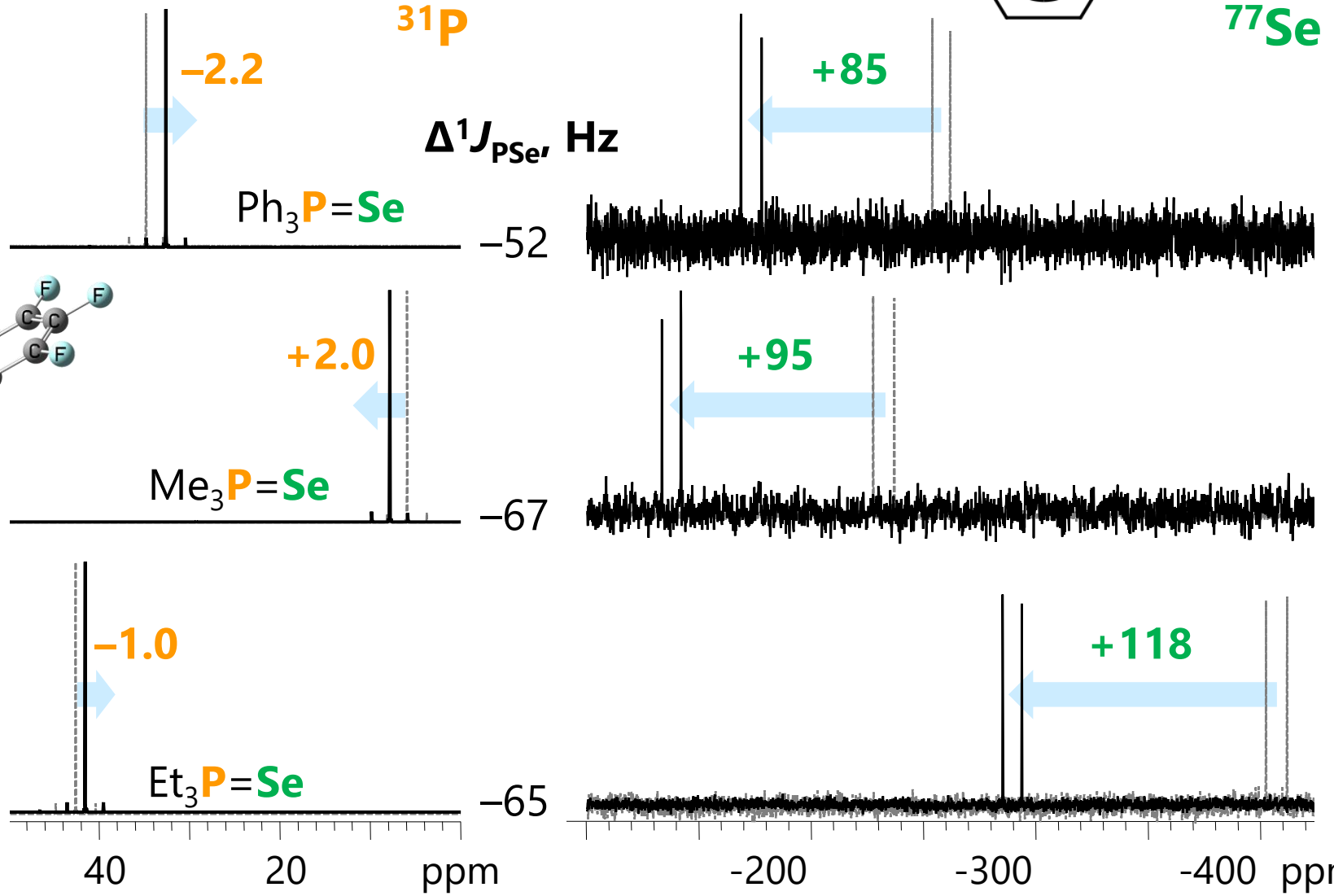
CD_2Cl_2, 180 K

Zakharov, A.S., *Phys. Chem. Chem. Phys.* (*under review*)

Phosphine selenides – probes for XBs

PW6B95-D3/def2-QZVP





Zakharov, A.S., *Phys. Chem. Chem. Phys.* (*under review*)

C_6F_5I, 298 K

Take home message

- Selenium-containing species are able to participate in σ-hole interactions and HBs. These NCIs are cooperative.
- NMR parameters of $R_3P{=}Se$ phosphine selenides (δSe, and $^1J_{PSe}$) are sensitive to subtle changes in the electronic environment of the P and Se atoms.
- Taking into account even a weak interactions with solvent molecules/neighboring residues/crystal field is extremely recommended for accurate modelling of selenium-containing systems.
- "Rich" ζ-splitted full electronic basis sets are recommended for NMR parameters.
- Promising NMR probe for NCIs in solution – *n*-$Bu_3P{=}Se$ and $Et_3P{=}Se$. In solid state – $Et_3P{=}Se$.

Thank you for your attention!