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Thermodynamically controlled Reactions of Selenenylphosphonium Ion $\text{Me}_3\text{PSeMe}^+$ toward Electrophiles and Nucleophiles

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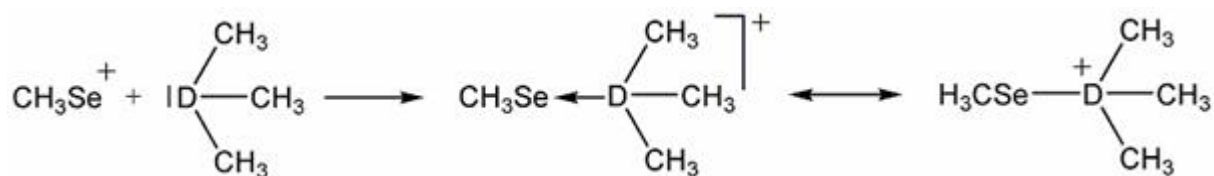
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Introduction

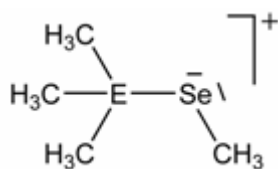
Lewis base adducts with selenenyl halides have been investigated experimentally and theoretically as models for interactions that might be relevant for the activity of Glutathione peroxidase (GPx).[1-3] Recently, we have shown that in donor adducts of selenenium ions with amines or phosphanes the formal donor-acceptor bond is covalent rather than dative.[4] Our findings suggested that in contrast to the description of adducts of the isolobal arsenium ions a description as selenenyl phosphonium and selenenyl ammonium ions appears more appropriate (Scheme 1). We also prepared compounds containing the selenenylphosphonium ion on a synthetic scale and studied their spectroscopic and chemical behaviour.[5] Here we describe *ab-initio* calculations exploring the reactivity of methyl substituted selenenyl phosphonium ions towards some simple nucleophiles and electrophiles.



Scheme 1: Resonance description of formal donor adducts of selenium ions (D = N, P).

Results and Discussion

To get a closer insight into the bond situation between phosphorus and selenium in selenenylphosphonium ions we performed *ab-initio* calculations using the program package Gaussian 03.[6] An interesting detail of the bond situation in **1** is the charge distribution within these cations. A comparison of the values obtained by Mulliken population analysis on HF and DFT level and natural charges obtained by NPA (DFT, MP2) are summarized in Table 1.



(1)

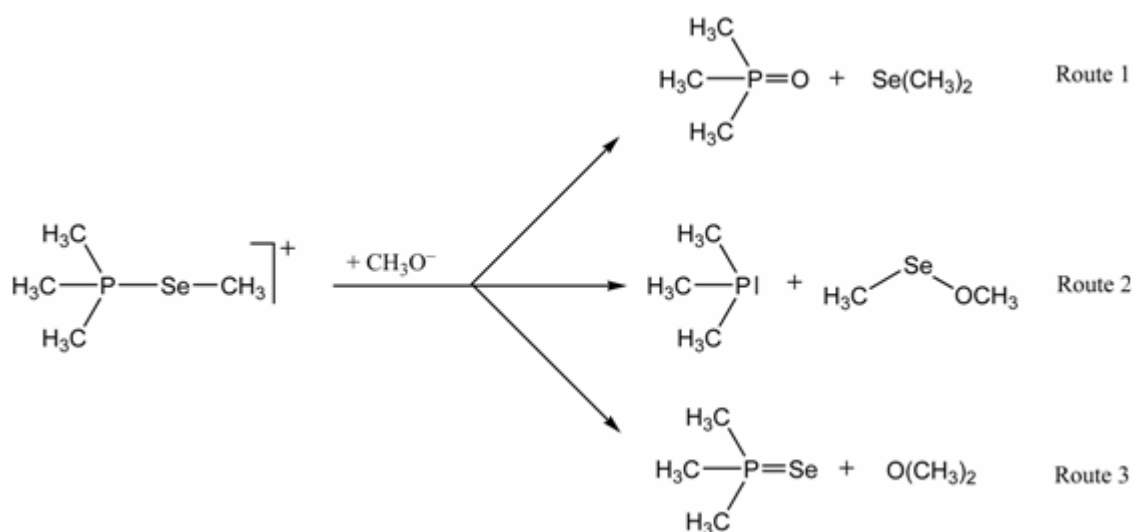
Table 1: Calculated charges of selected atoms in **1** at different levels of theory as indicated using a 6-311G(d) basis set.

	P	Se	Se-CH ₃	Se-CH ₃ ^a
HF	0.89	0.03	-0.77	0.08
B3LYP	0.70	0.13	-0.77	0.07
NBO B3LYP	1.27	0.16	-0.71	-0.04
NBO MP2	1.31	0.16	-0.72	-0.05

^a Charges of hydrogen atoms summed into carbon atoms.

On all levels of theory the positive charge in **1** is mainly located at the phosphorus atom. The value is lowest for a Mulliken analysis on DFT level ($q = 0.70$) and highest based on NPA ($q = 1.31$). In contrast, the selenium atom in **1** is almost neutral and carries only 3-19% of the charge of the phosphorus atom depending on the level of theory. At the carbon atom adjacent to selenium substantial negative charge is located which varies only slightly between $q = -0.71$ (NPA) and $q = -0.77$ (Mulliken). Much of this charge can be attributed to the hydrogen atoms bonded to this carbon atom. If the charge caused by the hydrogen atoms is subtracted, the methyl carbon atom appears with values between $q = -0.05$ (NPA) and $q = +0.08$ (Mulliken) almost uncharged. The close to neutral character of the

methyl carbon at selenium is noteworthy, because a potential description of **1** as a methyl cation stabilized by a selenophosphorane donor can be ruled out based on these findings.



Scheme 2: Hypothetical reaction pathways of **1** with $\text{H}_3\text{C}-\text{O}^-$.

To explore the reactivity of selenenyldiphosphonium ion **1** towards electrophilic and nucleophilic reagents we performed calculations on hypothetical reactions with simple electrophiles and nucleophiles. As a first example we studied the reaction of cation **1** with a simple nucleophile, the methoxide anion, which should give rise to uncharged products. Possible reaction products could arise from nucleophilic attack at the phosphorus atom (route 1), the selenium atom (route 2) or the methyl carbon atom (route 3). These routes are depicted in scheme 2 and the energies of the reactants and the respective products are summarized in table 2.

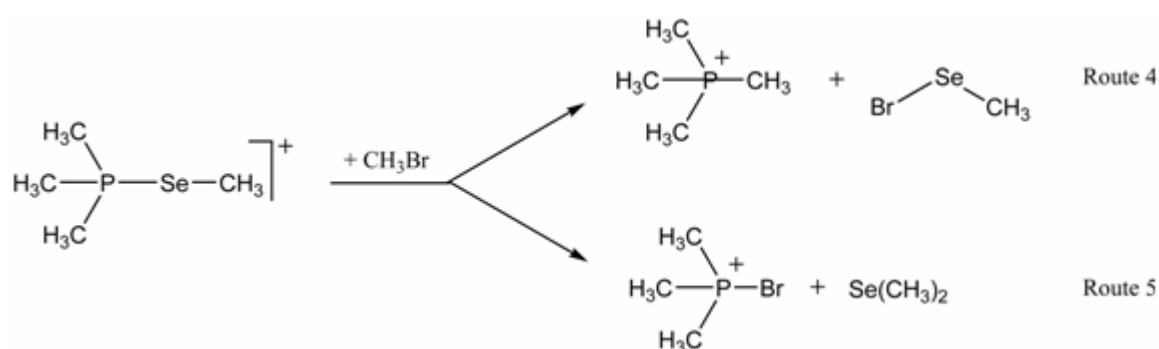
Table 2: Energies of reactants and products [hartree] and relative energies [kcal/mol] as outlined in Scheme 2.

	Reactants	Route 1	Route 2	Route 3	
HF//	-3013.2621184	-3013.4846483	-3013.5588104	-3013.5437544	hartree
6-311G(d)	0.00	-186.18	-139.64	-176.73	kcal/mol
B3LYP//	-3017.5272301	-3017.8193070	-3017.7512517	-3017.7953184	hartree
6-311G(d)	0.00	-183.28	-140.58	-170.93	kcal/mol
MP2//	-3014.3934465	-3014.6952625	-3014.6158471	-3014.6698692	hartree
6-311G(d)	0.00	-189.39	-139.56	-173.46	kcal/mol

In line with our previous interpretation of **1** as a selenenyldiphosphonium ion, the energetically most favored reaction pathway follows route 1 and is a consequence of a nucleophilic attack of the methoxide anion at the phosphonium

center in **1**. Nucleophilic attack at the methyl carbon atom would yield the products outlined in route 3 which are about 28 kcal/mol higher in energy than those obtained by route 1. The least favored of these three reactions is the one associated with nucleophilic attack at the selenium atom, which would correspond to the description as donor stabilized selenium ion. The energetic preference of a reactivity pattern as in route 1 again supports a description as selenenylphosphonium rather than as phosphane stabilized selenium ion which moreover is also the basis for the use of intermediate selenenylphosphonium ions as reagents for the preparation of selenol esters.[7]

We also wanted to explore the reactivity of **1** towards electrophilic reagents. Therefore we investigated the reaction of methyl bromide with **1**. The reaction of **1** with methyl bromide should bear a close resemblance to the reaction of **1** with methyl iodide. The latter is of interest since it might be relevant in the synthesis of **1**, if more than the exact equimolar amount of CH₃I is applied, or when during the addition of CH₃I a locally higher concentration of this reagent occurs. Since the 6-311g(d) basis set used in our study is available for bromine but not for iodine we performed the calculations with CH₃Br rather than with CH₃I. In principal, a potential electrophilic attack might occur at the selenium atom (route 4) or after dissociation of **1** into phosphane and selenenyl cation at the lone pair of phosphorus (route 5) as outlined in scheme 3. The energies of the reactants and the respective products are summarized in table 3. Unlike the reaction with H₃CO⁻, the energy differences in the reaction of **1** with H₃CBr are much smaller. The energetically most favored process is the formation of the tetramethyl phosphonium ion along with methyl selenenylbromide (route 4). Less than 10 kcal/mol higher in energy is the formation of Se(CH₃)₂ along with a bromo substituted phosphonium cation (route 5).



Scheme 3: Hypothetical reaction pathways of **1** with H₃C-Br.

Table 3: Energies of reactants and products [hartree] and relative energies [kcal/mol] as outlined in Scheme 3.

	Reactants	Route 4	Route 5	
HF/	-5510.8349578	-5510.8419100	-5510.8261485	hartree
6-311g*	0.00	-4.36	5.53	kcal/mol

B3LYP/	-5516.4827554	-5516.4898713	-5516.4744628	hartree
6-311g*	0.00	-4.47	5.20	kcal/mol
MP2/	-5511.8866738	-5511.8938103	-5511.8782147	hartree
6-311g*	0.00	-4.48	5.31	kcal/mol

In the reaction of **1** with CH₃Br the preference of route 4 is quite small and might be easily outweighed by solvation effects or other substrate specific parameters which are not included in these calculations. This latter possibility is actually corroborated by experimental evidence. We found, that an excess of methyl iodide in the formation of **2** leads to a slow decomposition of the selenenylphosphonium ion to (H₃C)₃SeI and selenium-free P(V) compounds, which corresponds to a reaction course as in route **5**.^[5] Generally, the results presented here refer only to thermodynamically controlled reactions.

Acknowledgements

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Computational Details

Quantum chemical calculations were carried out using the Gaussian03 suite of programs, employing a 6-311G(d) basis set on Hartree-Fock, MP2 and DFT(B3LYP) level.^[6] The optimized geometries were confirmed as minima on the potential surface by second-derivative calculations.

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