Homolytic Substitution on Selenium: Formation of Selenium-containing Heterocycles by Direct Carbon–Selenium Bond Formation

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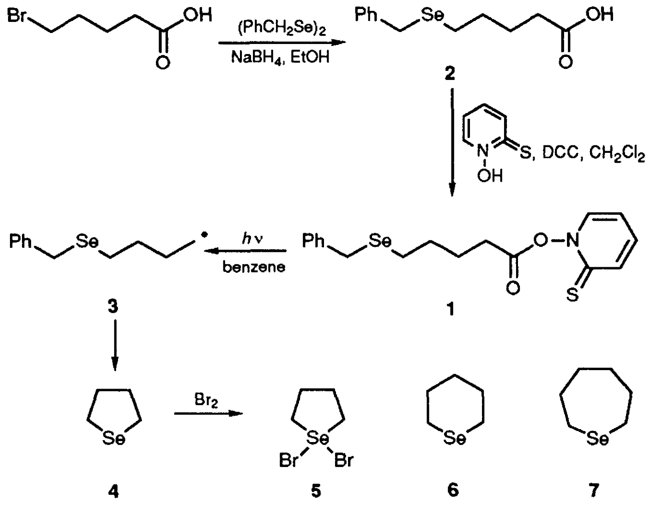
Thiohydroxamic esters derived from 5-(benzylseleno)pentanoic acid, 6-(benzylseleno)hexanoic acid and 7-(benzylseleno)heptanoic acid decompose smoothly upon irradiation, with the loss of carbon dioxide, to give tetrahydroselenophene, selenane and selenopane in good yield.

Heterocyclic ring formation by intramolecular homolytic substitution at sulfur in alkyl sulfides is a well documented procedure.[1] While this technique has been available for almost three decades, no work directed at similar homolytic processes at other heteroatoms has, to the best of our knowledge, been reported. In an attempt to expand the synthetic utility of homolytic substitution reactions, we have examined the intramolecular attack by carbon-centred free radicals at a selenium atom with the aim of preparing 5-, 6- and 7-membered selenium-containing rings. To that end, the



Scheme 1

thiohydroxamic ester derivative[2] **1** of 5-(benzylseleno)pentanoic acid[3] **2** was prepared according to Scheme 1. Thus, 5-bromopentanoic acid was treated with dibenzyl diselenide–sodium borohydride in ethanol to give **2** which in turn was converted to the bright yellow thiohydroxamic ester **1** by the action of *N*-hydroxypyridine-2-thione and dicyclohexylcarbodiimide (DCC) in dichloromethane in quantitative yield.

We chose to use the thiohydroxamic ester procedure of Barton,[2] as the required radical **3** could be generated without the need for chain carriers such as tri-n-butyltin or tris(trimethylsilyl)silyl radicals, species known to attack both alkyl selenides and alkyl bromides.[4,5] Indeed, it is our experience that tri-n-butyltin hydride reduces molecules containing both the phenyl selenide and bromide moiety without discrimination.

When the thiohydroxamic ester **1** was dissolved in [$^2H_6$]benzene† in an NMR experiment and the sample irradiated with a 150 W tungsten lamp, the solution became colourless after 5 min. 270 MHz ^1H NMR spectroscopy indicated the formation of tetrahydroselenophene[6,7] **4** in 79% yield, clearly demonstrating the efficiency of the homolytic substitution process on selenium.

When the procedure was repeated on a preparative scale, we were unable to isolate **4** either by distillation or preparative GC, as **4** appeared to co-distil[7] with the reaction solvent or decompose on the column. We eventually chose to characterize **4** by conversion to the stable crystalline 1,1-dibromotetrahydroselenophene[6] **5**. Thus, the crude reaction mixture was poured onto a flash-chromatography column and **4** eluted with hexane. Bromination was achieved by the dropwise addition of bromine in carbon tetrachloride. Removal of the solvent gave **5** in 74% yield.

In similar fashion, 6-(benzylseleno)hexanoic acid[3] was converted into selenane[8] **6** in 78% yield‡ and isolated as the crystalline 1,1-dibromide[8] in 69% yield, while 7-(benzylseleno)heptanoic acid[3] was converted into selenopane[9] **7** in 50% yield.‡

When the preparation of **7** was repeated on a preparative scale, extensive formation of a white precipitate was observed. Attempted isolation of **7** as its 1,1-dibromide in the usual way yielded no product. Compound **7** is known to polymerize[9] readily.

These results represent the quickest and highest yielding procedures for the formation of these selenium-containing ring systems.

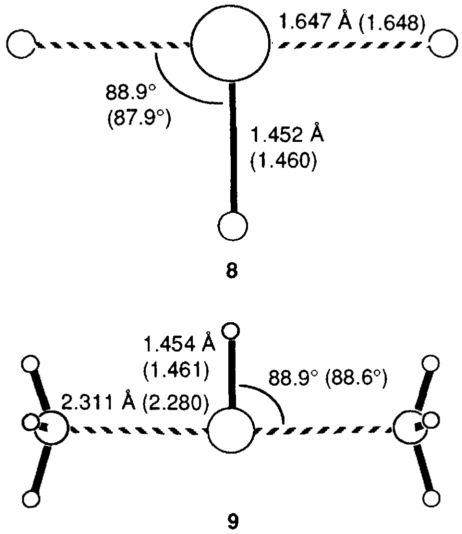


Fig. 1 UHF/HUZ-SV**-calculated transition structures for the homolytic substitution of H• on H_2Se and •CH_3 on CH_3SeH [3-21G(*) data in parentheses]

Very little is known about the mechanism of the homolytic substitution process at either sulfur or selenium. Beckwith and Boate[10] argued that the reaction probably proceeds through a colinear (S_H2) transition state or an intermediate in which the rate of pseudorotation is slow with respect to the departure of the leaving group, in order to explain the strict inversion of configuration they observed in chiral sulfoxides. Chatgilialoglu and coworkers[5] suggested an intermediate in the attack of tris(trimethylsilyl)silyl radical on alkyl phenyl selenides in order to explain their observed product ratios. We are only aware of two reports in which homolytic substitution by a carbon-centred radical on selenium has been used. One used diphenyl diselenide to trap an alkyl radical,[11] while the other demonstrated that alkyl phenyl selenides become involved in atom-transfer reactions.[12]

In order to shed some light on this mechanistic problem, we have examined the reaction of hydrogen atom with hydrogen selenide and the methyl radical with methaneselenol using *ab initio* molecular orbital theory. Ground and transition states were located in the usual way[13,14] using the 3-21G(*)[15] and HUZ-SV**[16]§ basis sets at the UHF level of theory. Single point MP2[13] calculations were performed on the optimized structures at the higher level of theory in order to assess the importance of electron correlation.

No intermediate that might be involved in the homolytic substitution process could be located on the potential energy surface for either reaction. The T-shaped transition structures **8** and **9** corresponding to the expected S_H2 reaction were, however, located at both levels of theory and are depicted in Fig. 1. The evaluation of the complete set of harmonic frequencies for both **8** and **9** proved that they are indeed the correct transition structures.

The energy barriers were calculated to be 67.4 and 73.6 kJ mol^{-1} at the lower and higher levels of theory respectively for the formation of **8** and 78.2 and 95.4 kJ mol^{-1} [3-21G(*) and HUZ-SV** respectively] for the formation of **9**. Single-point MP2 correlation correction (MP2/HUZ-SV**//UHF/HUZ-SV**) resulted in barriers of 55.6 and 76.6 kJ mol^{-1} for the formation of **7** and **8** respectively.

Inspection of Fig. 1 reveals that **8** and **9** are indeed as suggested by Beckwith[10] for the transition state proposed for the homolytic substitution process on sulfur.

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† *Ca.* 20 mg of **1** in 1 ml of solvent.

‡ NMR yield.

§ The HUZ-SV** basis set used in this study is Huzinaga's[16] Se/43321/4321/41//C/421/31/1, split valence + polarization on Se and C with the Dunning/Huzinaga D95V[16] valence double zeta + polarization basis for H.

We are currently investigating the scope of this procedure for the synthesis of other selenium-containing heterocycles and the mechanistic details of other homolytic substitution reactions by *ab initio* molecular orbital theory.

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