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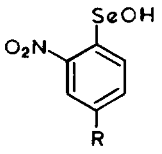
"STABLE" SELENENIC ACIDS

Hans J. Reich*, William W. Willis, Jr., and Susan Wollowitz
McElvain Laboratories of Organic Chemistry, Department of Chemistry,
University of Wisconsin, Madison, Wisconsin 53706

Abstract: Two of the stable selenenic acids reported in the literature are actually other materials.

Selenenic acids are believed to be transient intermediates in a number of reactions involving redox processes at selenium, most notably the selenoxide syn elimination[1], and the reduction of seleninic acids[1b,2] as well as the oxidation of diselenides[1b,3]. The rationale for postulating selenenic acids as reactive intermediates is based in part on analogy with the more extensively studied sulfur analogs, but mainly on the reports that a number of selenenic acids (1-4) were stable enough for isolation[4], among them a series of o-nitrobenzeneselenenic acids (1).[4a] Since the characterization of some of these compounds was rather limited, we have reinvestigated them and report our results here.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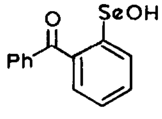
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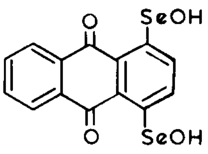
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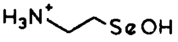
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The literature preparation of a material (A) originally assigned structure 1, R=H (reduction of o-nitrobenzeneseleninic acid with hydrazine)[4a] proceeds as reported, and gives a compound whose spectral properties[5a] are not inconsistent with the assigned structure. To confirm the assignment we observed by NMR spectroscopy the decomposition of o-nitrophenyl ethyl selenoxide (5) in chloroform and acetone, with the results shown in Figures 1 and 2. To our surprise, the first formed product from the elimination is not the putative "selenenic acid" A, but another material (B) with similar but quite distinct spectroscopic properties,[5b] which we believe is actually the selenenic acid 1 (R=H). This material is reasonably stable in solution, but is converted at varying rates (depending on reaction conditions) to compound A, disproportionation products, and/or products ($ArSeCH_2CH_2OH$, $ArSeCH_2CH_2OSeAr$) resulting from electrophilic addition[1b] to the ethylene present.

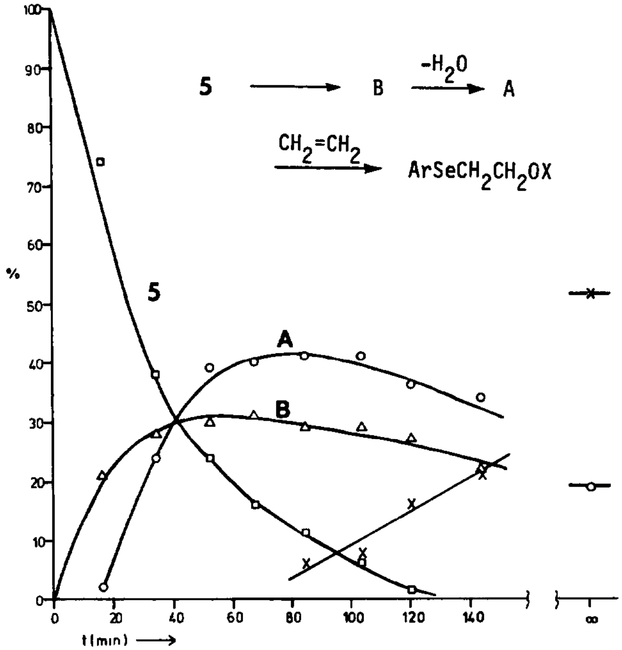


Figure 1. Decomposition of 5 in CDCl$_3$ at 38°C.

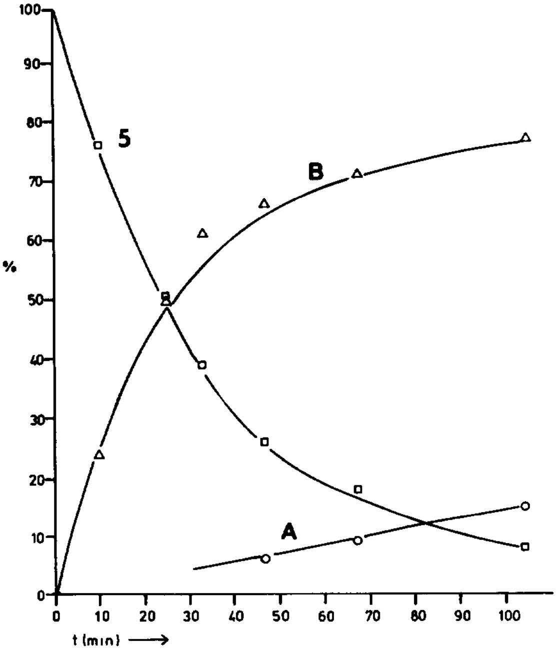
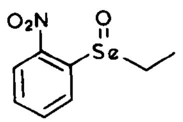


Figure 2. Decomposition of 5 in acetone-d$_6$ at 25°C.

What is the structure of compound A, previously believed to be the selenenic acid? Several lines of evidence have led us to conclude that A has the selenenic anhydride structure 6. The NMR spectra show a single set of four nonequivalent aromatic protons[5a] and a single ^{77}Se resonance at 1095 ppm, close to the resonance at 1066 ppm for B (1, R=H). These spectral data rule out structure 7, the selenolseleninate isomer of 6, since the number of ^{1}H and ^{77}Se resonances should be double that observed. Even a rapidly equilibrating form of 7 would not exhibit the average ^{77}Se NMR chemical shift observed for A.[6] If A is dissolved in acetone-d$_6$ or DMSO-d$_6$ containing 10% D$_2$O, it is slowly converted over a period of several hours to B, a reaction which we interpret as the hydrolysis of the anhydride 6. The C, H and Se elemental analysis of A fit for structure 6, but are well outside of experimental error for structure 1 (R=H). Finally, by carrying out the elimination of ethyl o-nitrophenyl selenoxide in aqueous acetone followed by the addition of more water we have been able to isolate compound 1 (R=H) approximately 80% pure.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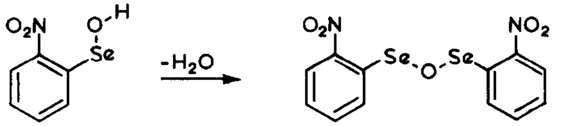
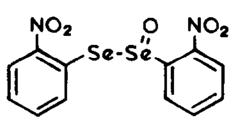


B = 1 **A = 6**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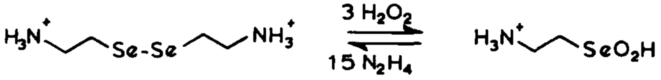
The original procedure for the preparation of 1 actually gives a mixture of 1 and 6 as a crude product, but the purification by recrystallization from refluxing benzene completes the dehydration to 6. It remains to be determined whether the other "selenenic acids" (1, R = CH_3, Cl, Br, OCH_3, NO_2) prepared by the same procedure as 1 (R=H) are selenenic acids or selenenic anhydrides. Although they have been postulated as reactive intermediates,[1b,3b] compound 6 is the first stable selenenic anhydride to be characterized as such.

Similar conclusions to those above for compounds 1 (R=H) and 2 have been made by Kice, McAfee and Slebocka-Tilk[8] based on spectroscopic studies of the reactions with water and alkanethiols.

2-Aminoethaneselenenic acid (4)[4d] is one of the most interesting of the "stable" selenenic acids reported because it lacks the structural features present in the other compounds, and because of its similarity to the selenium functionality believed to be present in one of the oxidation states of the selenoenzyme glutathione peroxidase.[9] We have reinvestigated the preparation of 4 and have established by spectroscopic measurements, elemental analysis, and redox stoichiometry that the material so identified is actually the corresponding seleninic acid 9. Oxidation of diselenide 8 with the calculated amount (1 equiv.) of hydrogen peroxide needed to convert it to the selenenic acid (4) gave a 2:1 ratio of 8 and 9, 3 equivalents gave complete conversion to 9 with no detectable intermediates. Similarly, reduction of 9 with hydrazine gave only diselenide 8. The presumed intermediate selenenic acid (4) in these reactions thus has a lifetime of at most a few minutes in water at room temperature, or is both reduced and oxidized more easily than 9 and 8, respectively.



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The results reported here, together with those of Kice, et al.[8] suggest that, with the possible exception of compound 3, no selenenic acid has been isolated in pure form, although compound 1 (R=H) is stable in dilute solution, and can probably be isolated.

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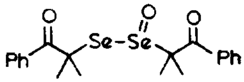
5. (a) Compound A (6): ^{1}H NMR (270 MHz, CD$_3$COCD$_3$): δ7.67 (ddd, J = 8.4, 7.0, 1.6 Hz, 1H), 8.09 (td, J = 7.1, 1.3 Hz, 1H), 8.24 (dd, J = 7.1, 1.6 Hz), 8.50 (dd, J = 8.4, 1.3 Hz, 1H). ^{77}Se NMR (CD$_3$COCD$_3$, ppm downfield from (CH$_3$)$_2$Se): δ 1095. *Anal.* Calcd for C$_{12}$H$_8$N$_2$O$_5$Se$_2$: C, 34.47, H, 1.93, N, 6.70. Found: C, 34.62, H, 2.01, N, 6.61.

(b) Compound B (1, R=H): ^{1}H NMR (270 MHz, CD$_3$OCD$_3$): δ 7.52 (ddd, J = 8.3, 7.1, 1.2 Hz, 1H), 7.88 (ddd, J = 8.3, 7.1, 1.5 Hz, 1H), 8.12 (dd, J = 8.3, 1.2 Hz, 1H), 8.33 (dd, J = 8.3, 1.5 Hz, 1H). ^{77}Se NMR (DE$_3$COCD$_3$): δ 1066. ^{13}C NMR (CD$_3$SOCD$_3$): δ 124.3, 125.2, 126.5, 135.5, 141.0.

6. Two selenolseleninates have been spectroscopically characterized[7]; ^{77}Se NMR (CD$_2$Cl$_2$): i (-80°C): 862 and 540 ppm, ii (-56°C): 693 and 273 ppm.



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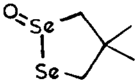

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