

Chiral Recognition of Selenoacid by ^{77}Se NMR

F. Hallwass*, R. O. Silva, S. M. C. Gonçalves, P. H. Menezes,
L. W. Bieber, A. M. Simas

Departamento de Química Fundamental – UFPE – Recife, Pernambuco, Brazil
hallwass@ufpe.br

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Abstract: *Chiral recognition, the ability of one chiral molecule to somewhat “recognize” the chirality of another, has been mostly studied in the liquid phase. Spectral differences between enantiomers in a chiral environment can be detected by NMR. ^{77}Se NMR spectroscopy can be used for the determination of enantiomeric excess. The methodologies involving ^{77}Se NMR have decisive advantages when compared to ^{13}C NMR. Several ^{77}Se NMR experiments were performed by titrating a sample of racemic selenoacid with the chiral solvating agent (CSA), methylbenzylamine, MBA, followed by acquisition of ^{77}Se NMR spectra. We observed the appearance of two anisochronous resonances, with a relatively large separation, from 37 to 56 Hz, corresponding to the formation of the diastereomeric complexes. This methodology avoids derivatization processes, and the studied compound can be easily recovered from the NMR tube.*

Chiral recognition, the ability of one chiral molecule to somewhat “recognize” chirality of another, has been mostly studied in the liquid phase. A number of methods have been employed to detect diastereomeric interactions in solution.¹ These methods reveal spectral differences between enantiomers in a chiral environment. Notably, NMR spectroscopy is a sensitive probe for the occurrence of these interactions. Chiral solvating agents (CSA) induce enantiomeric nonequivalence in the NMR spectra of a host of solutes. Depending on the intensity of the CSA/solute interaction, separated anisochronous signals can be detected.

^{77}Se NMR spectroscopy has already been used for the determination of enantiomeric excess, more specifically for the assignment of absolute configurations of acids and acid chlorides, aminoacids, and alcohols.² The methodologies involving ^{77}Se NMR have equation yielding the diastereomeric complexes formation and part of the ^{77}Se NMR spectra, before and after the addition of MBA as the CSA..

decisive advantages when compared to ^{13}C NMR: the sensitivity of ^{77}Se nucleus is three times higher than that of ^{13}C , and its natural abundance is 7.5%. Besides, selenium is very sensitive to its electronic environment and possesses a large chemical shift (δ) range (approximately 3400 ppm).³

Recently, we have described an efficient methodology for the preparation of chiral organoseleno acids (Figure 1).⁴ In order to accurately determine whether the reaction proceeded via an enantioselective pathway, we turned our attention to analyzing the enantiomeric composition of the obtained selenoacids. Our strategy was based on the formation of diastereomeric complexes, using CSA, (+)-methylbenzylamine [(+)-MBA], and detecting the resulting nonequivalence through ^{77}Se NMR. Figure 1 shows the chemical organoseleno acids appeared as a single peak at 462.8 ppm (1a). After the addition of

The experiments were performed by titrating the racemic sample with the (+)-MBA followed by the acquisition of ^{77}Se NMR spectra. Before the addition of the CSA, racemic

increasing amounts of (+)-MBA, two separate anisochronous resonances appeared, with separation between the signals of 36 Hz. A subsequent experiment performed that used

(-)-MBA, instead of (+)-MBA, led to equivalent results, indicating that either one of the CSAs may be used.

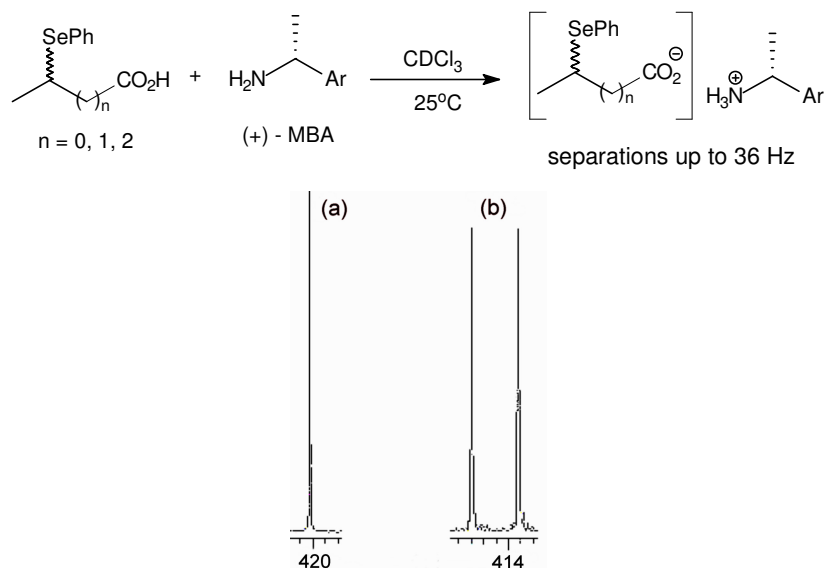


Figure 1. Above: reaction of the organoseleno acid and (+)-MBA yielding diastereomeric complexes. Below: ^{77}Se NMR spectra (a) before and (b) after addition of (+)-MBA.

We also confirmed the expected results that nonpolar solvents tend to increase the observed anisochrony, while polar solvents decrease it by solvating the diastereomeric complexes up to a point where $\Delta\delta_{R,S}$ tends to zero. This experiment was performed by adding small amounts of a polar solvent, $\text{DMSO-}d_6$, to the NMR tube containing the solute and (+)-MBA in CDCl_3 . A reduction of the signals separation was observed. On the other hand, when benzene- d_6 , a nonpolar solvent, was used instead, the separation between the two enantiomer signals increased by 19 Hz.

The effect of the variation of temperature, from -25° to 40°C , on $\Delta\delta_{R,S}$, was also studied.

Raising the temperature decreases the signal separation. To analyze its usefulness in determining enantiomeric purity of Se compounds, the methodology was extended to similar compounds where the carboxylic group was farther away from the seleno-chiral center (up to six bonds away from the selenium atom). Our results have shown that anisochrony is still preserved as far as five bonds away from the Se atom.

^{77}Se NMR spectra were obtained at 57.21 MHz on a Varian Unity plus spectrometer in CDCl_3 using diphenyldiselenide as an external reference ($\delta=463.0$). Typical parameters were as follows: pulse width 6 μs (45° flip angle),

10s recycle delay, 30 kHz spectral window and line broadening equal to 1.0 Hz. In summary, we have described a competitive alternative method for the enantiomeric analysis of chiral selenide compounds.

The methodology avoids derivatization processes, and the compound under investigation can be easily recovered from the NMR tube. Furthermore, either (+)-MBA or (-)-MBA can be used as chiral solvating agents. Moreover, the signals separation observed was relatively large, from 37 to 56 Hz, allowing a clean diastereomeric signal resolution.

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