NMR Spectroscopy Method for the Determination of Absolute Configuration of Chiral Thiols

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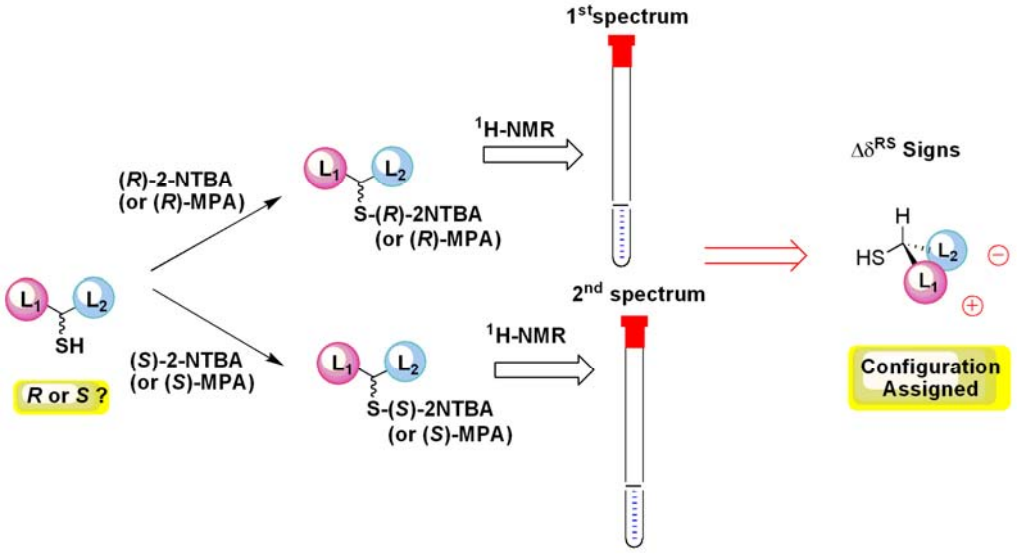
The assignment of the absolute configuration of chiral compounds by comparison of the NMR spectra of their derivatives with the (*R*)- and (*S*)-enantiomers of selected auxiliary reagents is a well-stablished methodology due to its reliability and simplicity. Chiral substrates that are amenable to treatment with these methods include monofunctional (i.e. primary and secondary alcohols, primary amines, cyanohydrins, etc.) and polyfunctional compounds (i.e. diols, triols, aminoalcohols).[1]

Herein, we describe a new method to assign the configuration of chiral secondary thiols that requires derivatization of the thiol with the two enantiomers of 2-methoxy-2-phenylacetic acid (MPA) and comparison of the ^{1}H NMR spectra of the corresponding diastereomeric thioesters. In addition, the new and more efficient reagent 2-tert-butoxy-2-(2-naphthyl)acetic acid (2-NTBA) is presented.[2]



Experimental (chemical shifts analysis, low-temperature NMR, selective formation of metal complex) and theoretical (energy calculations) data corroborate the correlation between the chemical shifts of those derivatives and their absolute stereochemistry.

[1] Seco, J.M.; Quiñoá, E.; Riguera, R. *Chem. Rev.*, **2004**, *5*, 17-118.
[2] Porto, S.; Seco, J.M.; Ortiz, A.; Quiñoá, E.; Riguera, R. *Org. Lett.*, **2007**, *9*, 5015-5018.

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