Computational Study on the Formation of *N*-spiro bis-Aziridinium Ions and Their Nucleophile-induced Ring Opening Reactions

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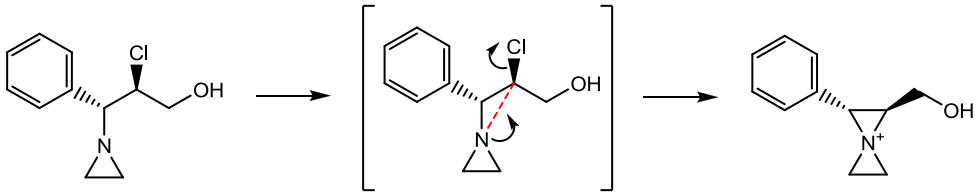
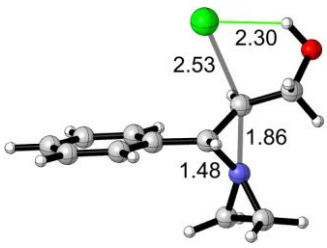
N-spiro bis-aziridinium ions are highly strained spiro-intermediates activated towards nucleophile-induced ring opening. Although their existence has been postulated in order to explain the outcome of certain reactions [1], their formation seems kinetically and thermodynamically too unfavorable to yield viable intermediates. DFT calculations were carried out to evaluate these claims.

The intramolecular nucleophilic subsitution of chloride by the aziridine nitrogen atom in 1-(2-chloroalkyl)aziridines results in the formation of *N*-spiro bis-aziridinium ions. This formation reaction is the rate-determining step in any reaction sequence involving these types of intermediates and seems to be promoted by polar solvent interactions and intramolecular hydrogen bonding between chloride and the hydroxyl group.

To account for the solvent influence, optimizations and energy refinements were performed using either no solvation, a polarizable continuum model (PCM), a supermolecule model with explicit solvent molecules or a combination of the last two. An extensive set of functionals (B3LYP, CAM-B3LYP, ωB97X-D, MPW1B95, BMK, M06-2X) was considered in these calculations. Intramolecular hydrogen bonding is a key factor in the stability of the *N*-spiro bis-aziridinium intermediates considered and eliminates the need for solvation with explicit solvent molecules.

Selecting PCM geometry optimizations as the method of choice, chloride was replaced by more or less potent leaving groups to reveal that in the case of good leaving groups the formation reaction is kinetically and thermodynamically viable.





References:
1. Mollet, K.; D'hooghe, M.; De Kimpe, N. *Journal of Organic Chemistry*, 76 (2011) 264-269.