VICINAL DIAMINES THROUGH N-ACTIVATED CHIRAL AZIRIDINES: SYNTHESIS AND CONCEPTUAL DFT STUDY

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N-Activated aziridines are versatile synthetic intermediates easily produced from β-amino-alcohols. Stereo and regio-controlled nucleophilic opening of aziridines leads to highly valuable, 1,2-bifunctionalized chiral compounds and among them, vicinal diamines are readily obtained. Beside its interest in medicine and pharmacy, the 1,2-diamine moiety has taken a large place as chiral ligands in transition-metal catalyzed asymmetric synthesis. We expose here a stereoselective synthesis of β-diamines through different types of activated aziridines and a theoretical rationalization of their regiospecific ring-opening by various nucleophiles.

Anti-configured diamines were synthesized from amino alcohols through trans-dibenzylaziridinium intermediates, regiospecifically opened at the benzylic position by benzylamine or ammonia. Syn-diamines were alternatively obtained either from the nosyl (i.e. nitrobenzenesulfonyl) or the HCl activated cis-aziridines derived from the same amino alcohols. The regioselectivity of these ring-opening reactions were both experimentally and theoretically investigated for the three activation methods. Experimental data (from [1H-13C] NMR) shows a clear preferred reaction at the benzylic position (C2) for both aziridinium species (H2+ and (Bn)2+). Interestingly, an inversion of regioselectivity is observed when aziridines are nosyl activated. This kind of inversion has already been reported between HBr and benzyl bromide activated aziridines. DFT calculations were performed in order to visualize LUMO’s and nucleophilic Fukui functions, and evaluate whether these are better localized near C2 or C3. FMO theory suggests that a site where the LUMO is localized is an electrophilic site, capable of accepting electronic density from the nucleophile’s HOMO. In parallel, a large positive value of the Fukui function (Eq. 1) indicates a good reactive site towards nucleophilic attack. Our calculations succeeded to explain and rationalize the experimentally observed regiochemistry, as LUMO’s and Fukui functions are mostly located on C2 for aziridiniums; whereas a more balanced pattern between C2 and C3 is observed for nosyl aziridines. These results are in agreement with the experimental ratios of regioisomers.

References