

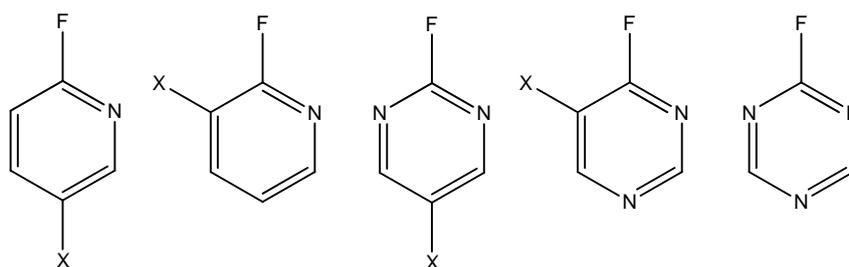
A BONDING EVOLUTION THEORY PERSPECTIVE OF THE aza-SNAr MECHANISM

Sebastián Gallardo-Fuentes^a, Sebastián Richter-Morales^a,
and Rodrigo Ormazabal-Toledo^{a,b}

^aDepartamento de Química, Facultad de Ciencias, Universidad de Chile, Casilla 653, Santiago, Chile

^bCentro Integrativo de Biología y Química Aplicada (CIBQA), Universidad Bernardo O'Higgins, Santiago 8370854, Chile

The electron density topology along the reaction pathway was analyzed to unravel the electron flow and bond rearrangements in the aza-SNAr reaction between amines and a set of 22 nitrogen-containing six-membered heterocycles bearing fluorine as leaving group (see Scheme 1). The analysis of the corresponding reaction profiles reveals that the aza-SNAr reaction can be nicely described as a variable $A_N + D_N$ mechanism, going from an unusual single-step pathway (for pyridine isomers) to the well-known two-step mechanism (for triazine isomers). There is a borderline zone involving a barrierless leaving-group departure step for diazine isomers fluoropyridazine, fluoropyrimidine and fluoropyrazine. The role of electronic structure of the heterocyclic ring along the reaction outcome was enlightened merging the physically elusive curly arrows picture with the elegant theory of dynamic systems.[1-2]



[1] Andres, J.; Gonzalez-Navarrete, P.; Safont, V. S.; Silvi, B. Curly arrows, Electron Flow, and Reaction Mechanisms from the Perspective of the Bonding Evolution Theory. *Phys. Chem. Chem. Phys.* **2017**, 19, 29031–29046.

[2] Krokidis, X.; Noury, S.; Silvi, B. Characterization of Elementary Chemical Processes by Catastrophe Theory. *J. Phys. Chem. A.* **1997**, 101, 7277–7282.