QSRR model of reactivity for Parham cyclization reactions

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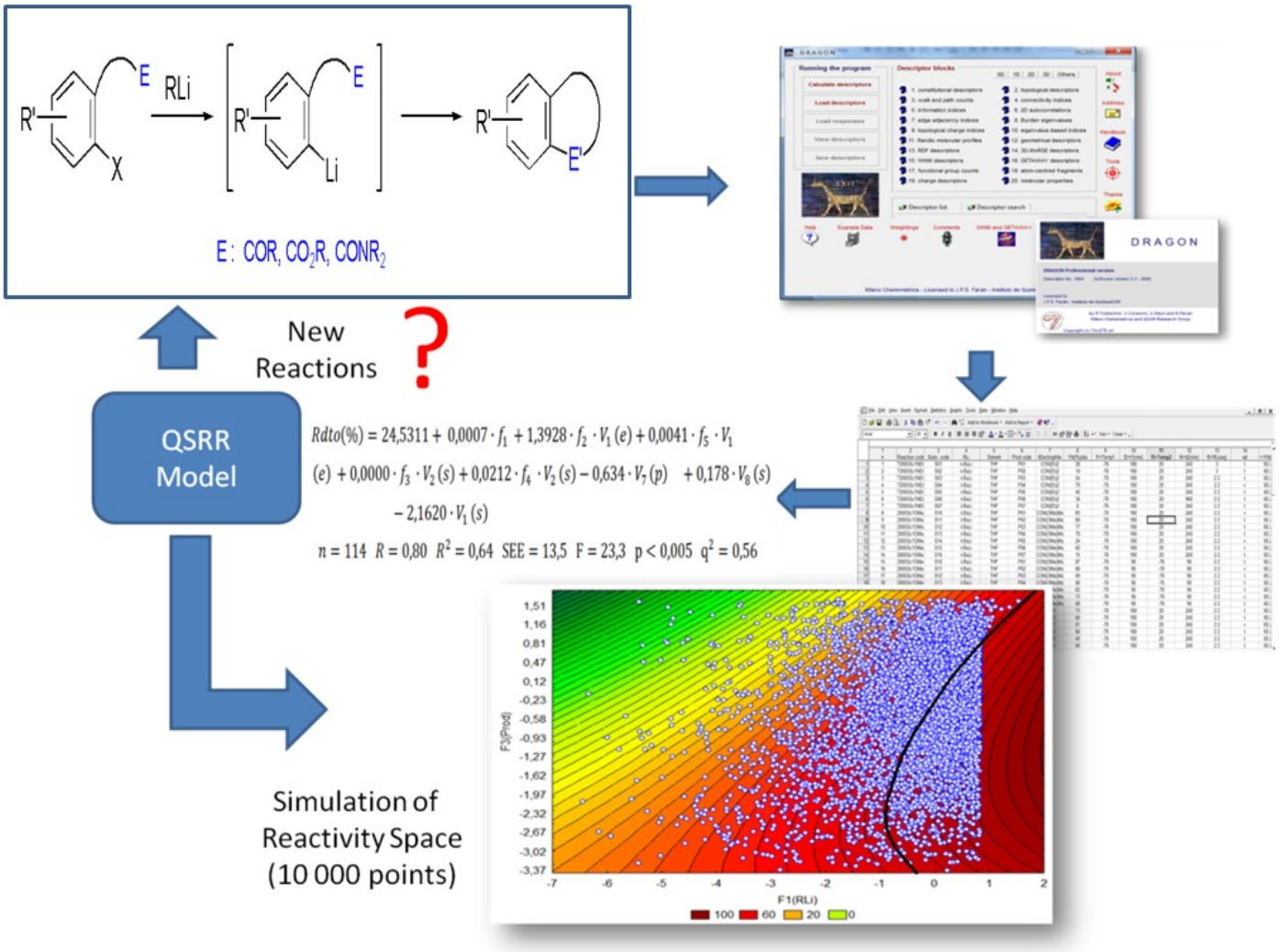

Abstract: Parham reaction is very important route for the synthesis of heterocyclic compounds, which consists of the intramolecular reaction of aryllithiums generated by lithium–halogen exchange with different types of internal electrophiles.[1]

In this paper we collected a dataset of >100 reactions for many substrates and internal electrophiles (mainly, amides and esters) with a wide range of reaction yields (0 – 99%). The reactions have been carried out in many different experimental conditions with different values non-structural variables (δ_k) like:

temperature of addition, addition time, organolithium equivalents, reaction times, and reaction temperature. Next, we calculated many structural and/or physicochemical variables (V_k) for the substrates and products of the reaction. After that, we constructed a Quantitative Structure-Reactivity Relationship (QSRR) model[2] able to predict the yield of reaction under many different conditions with acceptable accuracy. We also carried a 10.000-points simulation of the reaction conditions.

References

1. a) Ruiz, J.; Sotomayor, N.; Lete, E. *Org. Lett.* **2003**, *5*, 1115. b) Ruiz, J.; Ardeo, A.; Ignacio, R.; Sotomayor, N.; Lete, E. *Tetrahedron* **2005**, *61*, 3311. For a review, see: Sotomayor, N.; Lete, E. *Curr. Org. Chem.* **2003**, *7,* 275.
2. For related examples of our work; see:
a) Blázquez-Barbadillo, C.; Aranzamendi, E.; Coya, E.; Lete, E.; Sotomayor, N.; González-Díaz, H. *RSC Adv.* **2016**; *6*, 38602.
b) Aranzamendi, E.; Arrasate, S.; Lete, E.; Sotomayor, N.; González-Díaz, H. *ChemistryOpen* **2016,** http://dx.doi.org/10.1002/open.201600120.