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s-Triazine: A Multidisciplinary and International Journey †

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Abstract: 2,4,6-Trichloro-1,3,5-triazine (TCT) offers the unique ability to undergo sequential nucleophilic substitution reactions using regular nucleophiles (first Cl replacement at 0 °C, second at RT, and third at >90 °C), making s-triazine a privileged scaffold-finding application in drug development with an extension towards the development of new materials. This selective chemical property of TCT fulfills the goal of chemists to control organic structures and make them react in the required conditions for achieving each objective. In this regard, orthogonality and chemoselectivity are two modern organic chemistry concepts which have been exploited in various areas of research, ranging from supramolecular chemistry to organic/bioconjugation chemistry. We have demonstrated the fusion of these two concepts using TCT as "Orthogonal Chemoselectivity" and defined it as discrimination between reactive sites in any order. The usage of azide as one of the nucleophiles modulated the reactivity of the s-triazine core for the last Cl replacement. This allowed us to overcome the barrier of higher temperature (>90 °C) for the last Cl replacement which happened at RT, taking advantage of side chains of Cys, Tyr and Lys in a biological context. In this presentation, we revise the chemistry developed in our laboratories to manipulate the TCT core for application in our medicinal chemistry programs and in bioconjugation.

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