Tandem radical reactions of isonitriles: from concept to clinical trials

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Radical annulations of isonitriles were conceived in the early 1990’s in a typical setting of developing new synthetic methods. The chemistry was soon expanded to natural products synthesis, and—with the discovery of silatecan anticancer agents—to medicinal and combinatorial chemistry. The development of DB67, a first generation silatecan, will be traced from its discovery about a decade ago to its recent entry into clinical trials. The lecture will focus on small and large scale synthesis by using radical reactions, but will also delve into the mechanism of action of this family of anticancer agents, and present key aspects of preclinical development. The promise and problems of drug discovery and development in an academic setting will be highlighted.

1) PhNC
2) base

DB67, a topoisomerase I inhibitor

1996, synthesized by Dave Born
1998-2005, preclinical development by University of Kentucky
2006-2007, Phase I clinical trials