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EDITORIAL

Editorial

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Although MCR chemistry is as old as the beginning of organic chemistry when viewed as far back as pre-biotic times, the impact of this super fast and efficient chemistry has been only recently realized. In fact, a mere 10 years ago MCRs were often thought of as a niche chemistry with limited applications only in specialized areas. Interestingly, Ivar Ugi immediately recognized the full potential of the group of reactions named after him [1]. Indeed, he discovered the broad collection of Ugi reactions exactly 51 years ago and patented a first key application of this reaction, the one-step synthesis of the local anesthetic xylocain [2].

Nowadays the applications of MCR products span all the areas of the drug discovery value chain from preclinical discovery and development to clinical trials to marketed products. Several exemplary recent additions are shown in Figure 1. Almorexant is a first- and best-in-class Orexin 1 antagonist with promising results in the treatment of sleeping disorders and anxiety [3]. The compound was discovered by synthesizing directed libraries of Ugi-3CR products followed by a Pictet–Spengler reaction. GSK221149A is a potent, selective, and orally available Oxytocin antagonist which is currently undergoing advanced clinical trials to treat preterm labor. Pre-term labor occurs in 10% of all births worldwide and is the single largest cause of neonatal morbidity and death [4]. GSK221149A is synthesized by a key UDC transformation (*U*gi-*D*eprotection-*C*ylization). The latter technology was discovered and systematically developed enabling access to a wide array of pharmacologically relevant molecules and has been extensively adopted as methodology of choice for the preparation of widely used scaffolds by both the academic and private sectors [5, 6].

Praziquantel, although an old generic drug, remains of considerable importance and is required in large amounts to treat a hugely neglected tropical disease (NTD), Schistosomiasis (Note: there are >200 million people infected by this condition and Praziquantel is the only treatment option). Expedited access to the drug via lowering cost-of-goods (COG) of the active pharmaceutical ingredient (API) is clearly pivotal for expansion of the patient population receiving this therapeutic. As such, Praziquantel has been recently described as accessible via a very short 3-step process, which has potentially highly significant positive ramifications for dramatic increases in patient treatment [7].

Beyond pharmaceuticals, MCRs have found applications as molecular probes for biological systems, agrochemicals, and in material sciences. In view of this background of tremendous scientific activity in the field with an impressive breadth of utility, it is our pleasure to present this special issue mini section of *Molecular Diversity* that introduces two review articles from specialists in the field, coupled with several original articles. Specifically, Shaabani et al. extensively summarize the efforts towards basic and applied IMCR chemistry development (*I*sonitrile-based *M*ulti-*C*omponent *R*eactions) in Iran, entitled: "Recent progress of isocyanide-based multi-component reactions in Iran". The extensive review presents a plethora of enabling methodologies published by investigators in this region and represents the first review article to document the significant advances made in the MCR field by country specific-based institutions. The article nicely ties together a bolus of work and will be a 'must read' for MCR beginners and specialists alike.

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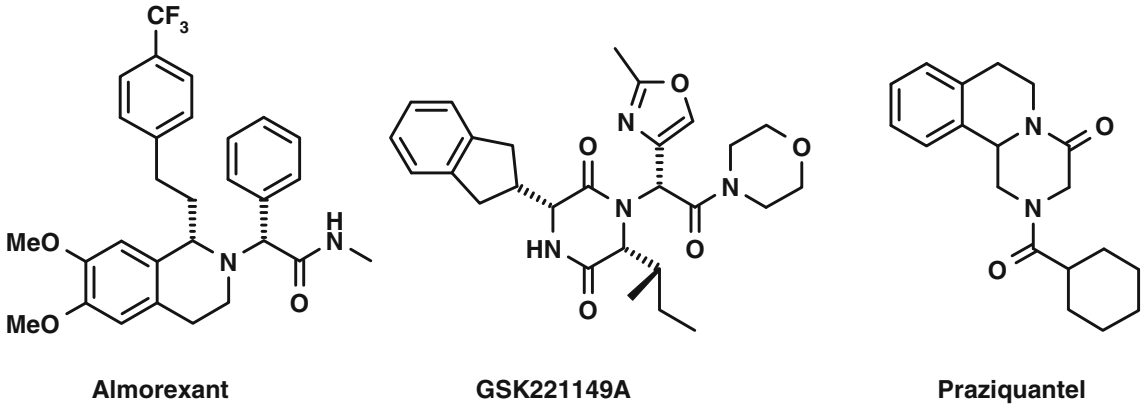

Fig. 1 Different new investigational new drugs in advanced clinical trials and the generic drug Praziquantel can be advantageously synthesized by MCRs

The second review by Huang and Dömling highlights recent progress in the Gewald three-component reaction (GW-3CR) of α-methylene nitriles, sulfur, and α-methylene ketones or aldehydes. The GW-3CR is best known for the efficient and short synthesis of the blockbuster atypical antipsychotic drug Olanzepine (Zyprexa^{TM}) with current sales in excess of US$ 5 billion per annum. Interestingly, the review also covers more recent applications of the GW-3CR, and it is expected the article will spur interest in a reaction with potentially tremendous, as of yet, undiscovered utility.

As previously noted, several original publications complete the special issue. The editors wish to thank all of the authors for their efforts in providing clear and comprehensive assessments of the many branches of the MCR arena covered herein and welcome the readers of *Molecular Diversity* to this enticing field of chemistry and its utility in expedited navigation of chemical space. Enjoy!!!

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