## SPECIAL FEATURE SECTION: ASYMMETRIC SYNTHESIS ON LARGE SCALE

# *Editorial*

## Uniting Asymmetric Synthesis and Scale-Up

The interest in chiral molecules has been well established for many years, especially in the pharmaceutical field. This has brought with it an ever increasing need for methodologies that allow the preparation of such compounds in high enantiopurity using procedures which allow efficient scale-up. Originally, the most straightforward and safest way to address this challenge was to revert to "classical" resolution techniques. However, the quest for improvements in the overall process economy and cost of goods has provided a strong driver to change to various enantioselective methods, ideally those which operate in a catalytic mode. In recent decades the academic world has been very active in the design and development of novel methodologies for conducting asymmetric transformations. Industry has responded well and has rapidly adopted many of these methods to tackle specific problems, often overcoming significant development problems in scale-up. Unfortunately, much of the successful industrial work in this arena has not been validated in commercial manufacture as many projects do not make it to this ultimate stage. As the state-of-the-art rapidly changes on both fronts, we felt it was time to focus an *Org. Process Res. Dev.* Special Feature on Asymmetric Synthesis on Large Scale and attempt to provide readers with a snapshot of recent work in this area from renowned academic and industrial groups.

The subject matter of the articles in this Special Feature is a good reflection of the diversity of this field, with a continuing trend towards more and more catalytic reactions. Much of the chemistry has been demonstrated on multi-kilogram scale. We feel that in principle this is also possible for the new chemistry reported by several academic groups. It is not surprising that hydrogenation is the key stereochemistry-defining operation in the largest number of contributions, as this is one of the richest areas in asymmetric synthesis. Examples include several catalytic asymmetric hydrogenations using a variety of novel ligands (J. G. de Vries et al. pp 585−591; M. Beller et al. pp 568−577; F. Spindler et al. pp 519−523; M. A. Schwindt et al. pp 524−533), as well as auxiliary-based diastereoselective hydrogenations (K. Lukin et al. pp 578−584; K. S. Gudmundsson et al. pp 539−545). Furthermore, there are two cases in which a dynamic kinetic resolution is the key to the success of the overall transformation (A. J. Blacker et al. pp 642−648; C. Chen et al. pp 616−623). A related contribution describes the enantioselective conjugate reduction of mixtures of nitro alkenes (E. M. Carreira et al. pp 633−636). The enantioselective desymmetrization of a prochiral substrate is a common denominator in the second-most abundant group of papers. Two contributions describe practical advances in the asymmetric ring-opening of cyclic anhydrides (Y. Furukawa et al. pp 609−615; C. Bolm et al. pp 592−597), whilst others highlight the ring-opening of a cyclic *meso*-epoxide (D. L. Varie et al. pp 546−559) and the promising intramolecular Stetter reaction of cyclohexadienones (T. Rovis et al. pp 598−604). Enzymatic processes remain an important option for the large-scale asymmetric synthesis of stereochemically complex molecules (H. Nanba et al. pp 503−508; M. Ikunaka pp 495−502). The same applies to the enantioselective phase-transfer catalyzed alkylation of glycine derivatives (K. Maruoka et al. pp 628−632; D. E. Patterson et al. pp 624−627). The remainder of the contributions describe a number of unrelated but important processes for the formation of carbon−carbon bonds. These include an auxiliary-controlled asymmetric acetate aldol reaction (J. J. Song et al. pp 534−538), the application of (*R*)-*p*-tolyl-methylsulfoxide in the synthesis of an epoxide (Z. Han et al. pp 605−608), the asymmetric addition of an aryl moiety to a benzaldehyde derivative (N. A. Magnus et al. pp 560−567), and both asymmetric and diastereoselective cyclopropanations (respectively M. Itagaki et al. pp 509−518 and E. D. Cleator et al. pp 637−641).

We hope that the examples of asymmetric synthesis which have been collected in this Special Feature will provide an accurate reflection of the current state of this important discipline. At the same time, we trust that this issue will inspire our colleagues in academia and industry to solve the many significant problems which remain.

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