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ScienceDirect
Tetrahedron
Tetrahedron 64 (2008) 4669–4670
www.elsevier.com/locate/tet

Preface

Research in natural product synthesis: a vital and dynamic global enterprise

The study of small molecule natural products (SMNPs) represents a cornerstone of organic chemistry[1] and such compounds remain a fascinating group, not least because of the remarkable array of intriguing structures that continue to be isolated from almost every conceivable source. Of course, the biological properties of many SMNPs mean that they can serve as leads for the development of new therapeutic agents.[1–3] Indeed, it has been estimated that at least 60% of the roughly 868 new therapeutic agents introduced worldwide over the last 20 years up to ca. 2003 have had their origins, in some way or another, in natural products chemistry.[4] Accordingly, natural products continue to attract the attention of synthetic chemists who often use these molecules as the inspiration for the development of new synthetic methodologies and/or strategies that might ultimately be deployed in a de novo total synthesis. There is a range of other possible motivations for undertaking such studies beyond the inherent intellectual satisfaction of completing a total synthesis of one of Mother Nature's beautiful molecules. Thus, it remains the case today that the absolute proof of the structure of a natural product may not be complete until a total synthesis of it has been achieved.[5] Others may be seeking to prepare a given natural product so as to then adjust its structure and thereby improve its therapeutic index, its chemical or its physical properties or some combination of all of these. Consequently, the total synthesis of natural products and related compounds remains as vital and as important an endeavor as it has ever been. Furthermore, in the 21st century the practitioners of this discipline are now well and truly spread across the globe. The intention of this Tetrahedron Symposium in Print (TSIP) is to try and highlight the world-wide nature of research in natural product synthesis through the assembly of a collection of papers produced by chemists working as far apart as Melbourne, Australia (Latitude 37° 47′ south) and York, England (Latitude 53° 58′ north).

It is interesting to reflect on the contents of the various papers presented here. Four of them, from the labs of David Evans (Harvard), Johann Mulzer (Vienna), Ian Paterson (Cambridge, UK), and Mark Rizzacasa (Melbourne), detail total syntheses of polyketide-type natural products and thus highlighting the continuing activity in this remarkably fertile area. The contribution from the Rizzacasa group is featured on the front cover of the hard copy version of this TSIP. A fifth paper from Mike Perkins' group, based at the Flinders University of South Australia, details some preliminary studies on the capacity of a linear triene to engage in an intramolecular (and presumably biomimetic) Diels–Alder reaction that produces a hexahydroindene unit resembling the core of the biogenetically unusual spiculoic acid-type polyketide. Other natural products incorporating aromatic residues and displaying fascinating biological properties are the atrochamins and epipyriculol and such compounds are the subject of papers from the labs of K. C. Nicolaou (Scripps, San Diego), and Steven Ley (Cambridge, UK), respectively. The northern-most research group featured in this issue, led by Richard Taylor (York, UK), details the synthesis of inthomycins A–C, aromatic heterocycle-containing natural products displaying both antimicrobial and herbicidal activity. One of the southern-most research groups contributing to this TSIP is based in Auckland, New Zealand and led by Margaret Brimble. Their paper is concerned with the synthesis of deoxy-analogues of the pyranonaphthoquinones eleutherin and thysanone. An approach to the synthesis of another quininoid natural product, komaroviquinone, is the subject of the contribution from Albert Padwa's group based at Emory University in Atlanta. Diterpenoids, in the form of C_{20}-gibberellins, are dealt with in a paper presented by Lew Mander's group (located at the Australian National University in Canberra) and some of their Japanese collaborators. Four of the remaining five contributions, specifically those from the groups of Samir Zard (CNRS, Palaiseau, France), Stephen Pyne (Wollongong, Australia), Phillip Kocienski (Leeds, UK), and Martin Banwell (Australian National University, Canberra) deal with the synthesis of alkaloids or their analogues. The last contribution to be mentioned here comes from the group of Herbert Waldmann (MPI Dortmund, Germany) and has a rather different 'flavor' from the rest. It deals with the synthesis of a dysidiolide-inspired compound library that has led to the discovery of novel AChE inhibitors. So, this contribution serves to emphasize the potential of natural products in developing new therapeutic agents.

I very much hope you, the reader, enjoy this diverse collection of papers that has been produced by a geographically well-dispersed group of organic chemists and their collaborators.

0040-4020/$ - see front matter
doi:10.1016/j.tet.2008.03.051

References and notes

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Available online 19 March 2008