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Preface

Natural Products in Medicinal Chemistry

The papers in this "Symposium in Print" (SIP) are the results of a request to both of us by Herbert Waldmann around 18 months ago, asking if we would be willing to ask (persuade or even cajole!) a number of researchers and their groups in various parts of the World to participate in this particular effort. It was designed as a way of transmitting information on a number of topics relevant to natural products chemists and their collaborators in a collegial manner, and also to allow them time and space to give their own views and results in a manner that permitted the authors to expand, nay, perhaps even expound, upon topics of interest both to them and to other scientists interested in the manifold ways in which natural products have impacted and continue to impact on all aspects of science.

There are 21 papers in all in this "Symposium in Print" and they cover a multitude of relevant topics. Since all natural products begin with biosynthesis, the SIP commences with four biosynthetic articles, with the first paper on the very prolific and interesting myxobacterial biosynthetic pathways by Weissman and Müller from Saarbrucken, Germany, followed in the same section by Kittendorf and Sherman from Michigan discussing the prototypical methymycin / pikromycin pathway, then Feng et al from Wisconsin covering production of isomigrastatin in heterologous hosts and finishing with the use of a new mass-spectral technique, Fourier transform ion resonance by Feng et al from Wyeth in New York, demonstrating how the biosynthetic pathways can be chemically and physically dissected in minute detail and on minute amounts of material.

The microbial world continues in the next three papers, leading off with a very interesting use of antisense techniques to isolate the fungal product Pleosporone by Zhang et al from Merck, Rahway, New Jersey, followed by the identification of a series of novel fungal Calmodulin inhibitors by Figueroa et al from the Universidad Nacional Autónoma de México in Mexico City, and completing this group, a thorough review of the novel proteasome inhibitor, salinosporamide A by Fenical et al from La Jolla / San Diego. The latter compound is the fastest compound yet described from discovery to phase I clinical trials in cancer.

Moving to the marine invertebrate environment (albeit the nominal source of the agents!), the next four papers demonstrate the different "chemistries" that are the hallmark of these sources. From soft Japanese corals, Yamashita et al from Tokyo show the presence of a novel antiangiogenic oxylipin, followed by their confreres from Northern Japan, Takahashi, Kubota and Kobayashi, who have expanded the nakijiquinones to now include the novel dimeric E and F analogues. The extension of the known agent Psammaplin A and its role as a more general activator of cell signaling is presented by McCulloch et al from the Utah group and Hickford, Blunt and Munro from the New Zealand group at the University of Canterbury, continue the marine saga with reports of four more halichondrins from the deep water *Lyssodendoryx*.

That the plant world has not been forgotten is shown by the next four articles, where Chapuis et al from the University of Virginia, describe the synthesis of modified acetogenins that potently inhibit mitochondrial complex I, followed by a report on aeroponically grown withaferin A derivatives by Xu et al from Arizona. Following this report from a hot arid climate, one then moves to a hot tropical area of the World , the island nation of Madagascar where Hou et al report on novel cardiac glycosides from plants collected in this environment. Continuing on the thrust of hot tropical climes, the final paper in the section by Pan et al reports on novel agents from Vietnamese plants.

The next paper is an interesting cross-match of microbial agents and intuitive chemical reasoning where Taldone, Sun and Chiosis from Memorial SloanKettering in New York City, report on the novel and potent agents that they synthesized as HSP 90 agents, derivatives of which are now in or approaching clinical trials without using computer assisted modeling.

Continuing in the synthetic vein, there are four papers covering a variety of natural product papers that show the advances in synthetic techniques that have arisen over the last decade or so, that now permit synthetic chemists to both confirm a structure and then make analogues that are not from Nature in some cases, but are definitively "derived from Nature". The section commences with an extensive review by Kumar, Mahajana and Chibale from Capetown, South Africa covering the synthetic medicinal chemistry related to natural product sourced antimalarial compounds and this is followed by a paper by Cao et al from Virginia Tech on the synthesis of marine sourced quinones with phosphatase inhibitory activities. Continuing in the marine synthetic arena, Paterson et al from Cambridge, UK next describe their synthetic approaches to variants of the very interesting marine compound dictyostatin and the section finishes with a review by Nicolaou, Chen and Dalby of the Scripps Institute in La Jolla that covers a wide-ranging series of compounds, demonstrating, yet again, that if a natural products chemist isolates a novel compound, there are synthetic chemists ready to exercize their talents in its complete synthesis. No longer is there a problem of supply in a significant number of cases due to the talents of the groups in this section.

Finally, the last paper is by Wilk, Waldmann and Kaiser from the Max Planck in Dortmund demonstrating yet again, that Nature provides "privileged structures" around which talented chemists can practice their art.

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David Newman
Gordon Cragg
Natural Products Branch, NCI

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