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Organic Chemistry in the –OMICs Era

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ABSTRACT: We are made to believe that we are in the age of the "BIO-" and "-OMICs", and that the time of organic chemistry has passed and there is nothing or very little left to be discovered. Wisdom dictates that this is far from the truth, although it does help organic chemists to realize that the days of "classical chemistry" are over and that they have to reshape their way of thinking and conducting research.

KEYWORDS: Organic chemistry, "OMICs" era, Scientist of the Millennium, Drug discovery, Interdisciplinary research projects.

Many chemistry departments in developed countries have lately been closed down, and many have changed their names in order to sound more interdisciplinary or more biology oriented. New names such as "Department of Chemistry and Chemical Biology", "Department of Biological Chemistry" or even "Department of Materials Science" have replaced the conventional "Department of Chemistry". This evolution is understandable because various disciplines including chemistry have integrated, and both teaching and research in science are gearing towards the interdisciplinary approach.

Chemistry had once been a very popular subject among scholars, the popularity probably reaching its peak during the period of the "Second Industrial Revolution". At the end of the year 1999, in an attempt to identify "Scientists of the Millennium", the journal ***Chemistry and Industry*** reported that 32 names had been proposed for deliberation and, eventually, voting. Astonishingly, seventeen of these candidates, or more than half, were either chemists or people who worked in chemistry related fields.[1] The final winners were of no surprise, Einstein and Newton were voted 1st and 2nd respectively, but, interestingly, the 3rd to 7th places were all won by chemists (Faraday, Pauling, Curie, Sanger, Lavoisier)!

The situation has gradually changed, and chemistry has increasingly been associated with the negative impact to the environment. It has suffered poor image in the media and bad reputation with the general public, up to the point where the word "chemistry" has turned to be a not-so-nice word. The change in attitude is also evident in other arena. In his article titled "Organic Synthesis - Where now?"[2], Professor Dieter Seebach quoted the comment of the then-editor of *Nature*, Professor John Maddox, who declared that chemistry had already lost its identity, citing as evidence the fact that the 1985 Nobel Prize for chemistry was awarded to two mathematicians! Interestingly, the 2006 Nobel Prize for chemistry was given to Professor Kornberg for his study of mRNA while the work by Drs. Watson and Crick on the structure of DNA, considered to be much more closely related to chemistry, was awarded the Nobel Prize in 1962 for physiology/medicine!

Many of us might have heard about the self-pitying opinions of some well known yet "resigned" chemists who believe that organic synthesis is already a "mature science" and that there is nothing or very little left to be discovered, that the time of chemistry has passed and we are at the beginning of the new era . . . . the age of the "BIO-" and "-OMICs".

Indeed, the time of conventional organic chemistry, be it organic synthesis or natural products chemistry, is over due to influence from the rapid advance of biomedical research. Hence, chemists just cannot afford to practice academic exercise by synthesizing a molecule or part of a molecule for the sake of "making" it or simply because it is interesting. It is now generally accepted that molecular function and activity are more important than the target chemical structures. Similarly, we can no longer conduct natural products research simply by investigating the chemical constituents of a living organism, be it plant or microorganism, identifying the chemical structure(s) followed by preparing a manuscript for publication, and concluding that we have completed our study on "drug discovery".

This particular issue was the topic of discussion at a meeting sponsored by the Thailand Research Fund, between several Thais and a high calibre group of Chinese chemists on 25 January 2007, where one of the questions raised for discussion is shown in the power-point (Figure 1). Until quite recently, research work which led to publication was considered work accomplished – but it was argued that the practice might not necessarily be applicable now because natural products research/drug discovery programs should

Research on Bioactive Natural Products (Drug Discovery)

1) Chemical Constituents
2) (in vitro) Bioactive Products, New Compounds
3) Publications
4) Then What ?

Fig 1. Powerpoint presentation from a Thai-Chinese meeting on 25 January 2007, sponsored by the Thailand Research Fund.

involve studies much further beyond the identification of new chemical structures.

Events in the sixties, when physical organic chemistry was extremely flourishing, should remind us of how those who are not well prepared and adapted to the rapid change in research trends are left in an abyss. Physical organic chemistry is still a very interesting and important subject, but it is not common nowadays to find an up-and-coming researcher working in this field. Chemistry is the central core of science and scientists have always valued its importance, consequently chemists have enjoyed the central role when collaborating with researchers in other disciplines. Scientific research is dynamic and is always moving forward, which results in new research interests and ideas, and also new methods of doing research. In the present -OMICs era, in order to tackle difficult problems, research projects tend to involve people from a variety of fields including chemists. It is, however, very disturbing to hear comments such as "the life-science people act as if they were all generals and we were foot-soldiers": this from a highly capable organic chemist working in an interdisciplinary research endeavor. This chemist should be reminded that if one thinks like a foot-soldier one will always be a foot-soldier!

What type of research in organic chemistry, then, is worth doing in this -OMICs era? Natural products chemistry and organic synthesis are always essential and worthwhile pursuing. Numerous important problems are waiting to be addressed and solved. However, the mission of the projects and the research methodology must be carefully planned with clear focus on specific aims. Project justification will be the most important criteria. Natural products research on drug discovery should involve the bioactivity guided isolation and identification technique, not the classical identification of chemical constituents.

The current research infrastructure and supporting grants are not unfavorable for those who want to do research on organic synthesis as compared to the situation of ten or twenty years ago. Organic synthesis is definitely not a "mature science" as mistakenly understood. World-renowned scientists[2-4] have identified many important research areas that should be of interest to synthetic chemists, for example, asymmetric hydrogenation, chiral synthesis and syntheses of synthetic enzymes, catalysts and chiral templates, including molecules of special interest to biology and materials science. Many aspects of the above mentioned topics can be done in this country and it is encouraging to note that many of our young chemists are working along this line.

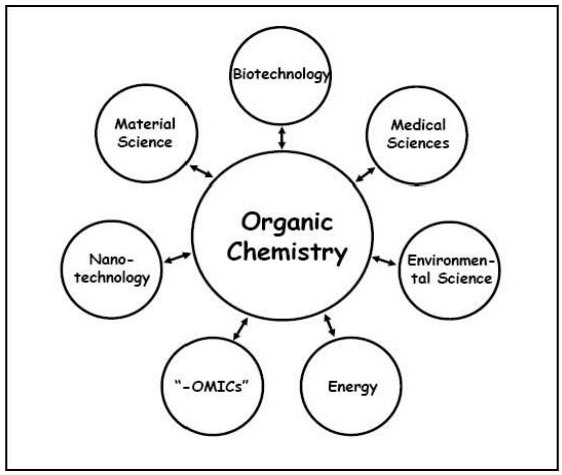

Fig 2. Roles of organic chemists in interdisciplinary projects.

As illustrated in the diagram (Figure 2), chemists will undisputedly play indispensable roles in the various interdisciplinary research projects. They must help to identify products from reactions and make or produce chemical compounds via their synthesis program. After all, chemists should recognize that, in order to carry out research to meet their objectives, these multidisciplinary programs will need organic compounds - lots and lots of them too!

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