OBC
www.rsc.org/obc

Profile

K. C. Nicolaou

Professor of Chemistry, The Scripps Research Institute and UC–San Diego

Organic & Biomolecular Chemistry **profiles Professor K. C. Nicolaou**

1969: Bedford College, University of London, UK, BSc (First Class)

1972: University College, University of London, UK, PhD, with Professors F. Sondheimer and P.J. Garratt

1972: Columbia University, New York, NY, Research Associate with Professor T.J. Katz

1973: Harvard University, Cambridge, MA, Research Associate with Professor E.J. Corey

1976: University of Pennsylvania, Assistant Professor of Chemistry

1980: University of Pennsylvania, Associate Professor of Chemistry

1981: University of Pennsylvania, Professor of Chemistry

1988: University of Pennsylvania, Rhodes-Thompson Professor of Chemistry

1989 to date: The Scripps Research Institute, La Jolla, California, Department Chairman, and Darlene Shiley Chair in Chemistry

1989 to date: University of California at San Diego, La Jolla, California, Professor of Chemistry

1996 to date: The Skaggs Institute for Chemical Biology, TSRI Aline W. and L.S. Skaggs Professor of Chemical Biology

K.C. Nicolaou was born on July 5, 1946, in Karavas, a small coastal town in northern Cyprus. He now lives in La Jolla, California with his wife, Georgette, and younger son, Paul Jason. Their older children Colette, Alex, and Christopher are pursuing higher degrees away from home but are still frequent visitors. La Jolla is beautifully situated north of San Diego on the California coast overlooking the Pacific Ocean, an area not so different in landscape from the Mediterranean town where he grew up. Besides sharing chemistry with his students, he enjoys walking on the beach, listening to music and reading about history and geopolitics.

When did you first realize that you wanted to work in chemistry?

At the age of fifteen I was inspired by a high school teacher in Nicosia, Cyprus. His mesmerizing style of teaching chemistry and demonstrating its power with stunning experiments convinced me that I wanted to make chemistry my lifelong career, and despite the many opportunities I had subsequently to go into other professions, I never abandoned my passion for chemical synthesis, an art I came to love both as a researcher and an educator.

Who was the first person to inspire your research?

As I alluded to above, it was my multi-talented chemistry teacher at the Pancyprian Gymnasium in Nicosia, Cyprus, Dr Telemachos Charalambous, who first introduced me to chemistry. My interest in chemical research was later enhanced by Dr Roger Bolton at Bedford College, London, with whom I carried out a research project as an undergraduate. Subsequently, of course, I was infused with further enthusiasm and passion for research by my PhD mentors Peter Garratt and Franz Sondheimer at University College, London, and by Thomas J. Katz and E.J. Corey with whom I conducted postdoctoral studies in the United States.

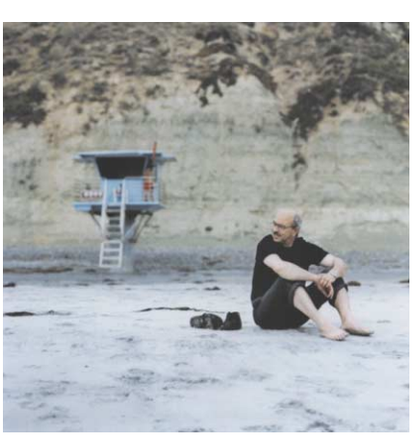
† Photographs show Professor Nicolaou, on the beach at La Jolla, with his research group, in the atrium of the Beckman Building for Chemical Sciences.

Tell us something about the areas of chemistry you are currently researching?

The main theme of our research is the same as it has always been, total synthesis, but with some new twists. At present it seems that endeavors in total synthesis will never end—for nature continues to provide us with amazing new structures endowed with biological activities and challenging molecular motifs. Fueled by the need to sharpen the tool of chemical synthesis and the relevance of this art and science to biotechnology and pharmaceutical research, total synthesis remains at center stage offering not only unique opportunities for discovery and invention, but also for the training of young men and women. Our aims are to reach Nature's complexity and diversity through innovative and efficient strategies and to mimic its chemistry and biology through our own designs.

Why did you decide to research in these areas of chemistry?

There is a strong element of art in total synthesis that appeals to me in a way that science alone may not. The ability to design and execute a strategy towards a diabolically complex and seemingly unapproachable molecule, and to create novel analogues of it, requires and demands the best in human ingenuity, dexterity and stamina. The opportunity to discover new chemistry and biology at the same time has the makings of an irresistible adventure, despite the often treacherous ground to be traversed before success. The rewards, however, are enormous both in terms of the benefits to humanity and the education of young scientists.



DOI: 10.1039/b301552c

Where would you like to see your research in both the short and long term?

Well, in the short term, I would like to see our ongoing projects in total synthesis come to fruition as expeditiously as possible and with a rich bounty of discoveries and inventions. In the long term, it is important to make long lasting contributions in chemical synthesis and chemical biology which, in turn, enable the drug discovery and development process for humanity's betterment.

What would you most like to achieve in your lifetime in chemistry?

I love the challenge of complex molecular architectures, whether natural or designed. From the synthesis point of view, the designs of Nature are much more sophisticated and stunning than those imagined by man. It is, therefore, not surprising that I adopted the total synthesis of natural products as my passion even though I began my chemistry career as a designer and synthesizer of theoretically interesting molecules. My ambition is to explore and understand the chemistry and biology of as many complex and diverse natural products as I can and to discover and invent as much new science in the process of synthesizing them in the laboratory, with my students, of course. Educating students in chemistry and seeing them blossom in their own space is perhaps an even higher honor and source of satisfaction for me, and I am extremely proud of all those who pass through my laboratories and spend time with me as collaborators.

What do you find most enjoyable about your job on a daily basis?

What is most exhilarating about my job is the opportunity to share with my students those moments of inspiration and success—whether the conception of a new idea, the making of a new discovery or the completion of a total synthesis. Looking at matching NMR spectra of natural and synthetic samples of a target molecule at the end of a total synthesis elicits deep and memorable feelings of excitement and wholehearted satisfaction. The journey itself with all the perilous traps and extreme challenges is also a source of stimulation and excitement. It is indeed a privilege to be able to share such moments with my students—the protagonists of such endeavors. The ultimate satisfaction, however, comes from the long lasting success of my students in their own careers.

What frequently annoys you about your job?

I have to say that the most frustrating moments in my experience are those accompanied by bad news on funding. Being a chemist, it is not always easy to give an appreciation or to explain the impact of our science to those higher up in government who have the power to make things happen. It is ironic that despite chemistry's central and decisive role in the pharmaceutical industry and biotechnology, our share of funding is much less that other disciplines. This situation can be particularly annoying when "trendy frontiers" take away the lion's share of funds at the expense of fundamental science which is sometimes erroneously viewed as classical, and, therefore, conventional. There is still so much to be discovered in basic science and we should not all rush for applied science and "trendy" areas of research—especially those of us in academia, for basic research still, and will always, underpin the applied sciences.

Which scientist/chemist do you most admire through history and why?

I must admit that I have a bias toward the classical Greeks, so I pick Demokritos, who defined the atomic theory, and Archimedes who was a true genius in so many areas. But I also enormously admire R.B. Woodward for his brilliance in the art of total synthesis. My esteem and respect also extends to my mentors who showed me what education and research are all about and how to pass the torch on to the next generation.

If you could successfully solve any scientific problem, what would it be and why?

Being able to design and expeditiously synthesize a high affinity ligand to any given biological target constitutes the holy grail of drug design. I would love to be able to solve this problem by computer modeling and automated chemical synthesis, a feat that will obviously require enormous power and greater depth of understanding in the fields of structural biology, computational chemistry and chemical synthesis. This could speed up the drug discovery and development process and bring us closer to our dream of eradicating pain and disease from the face of the earth.

Professor Nicolaou can be contacted at The Scripps Research Institute and the University of California, San Diego. Email: kcn@scripps.edu