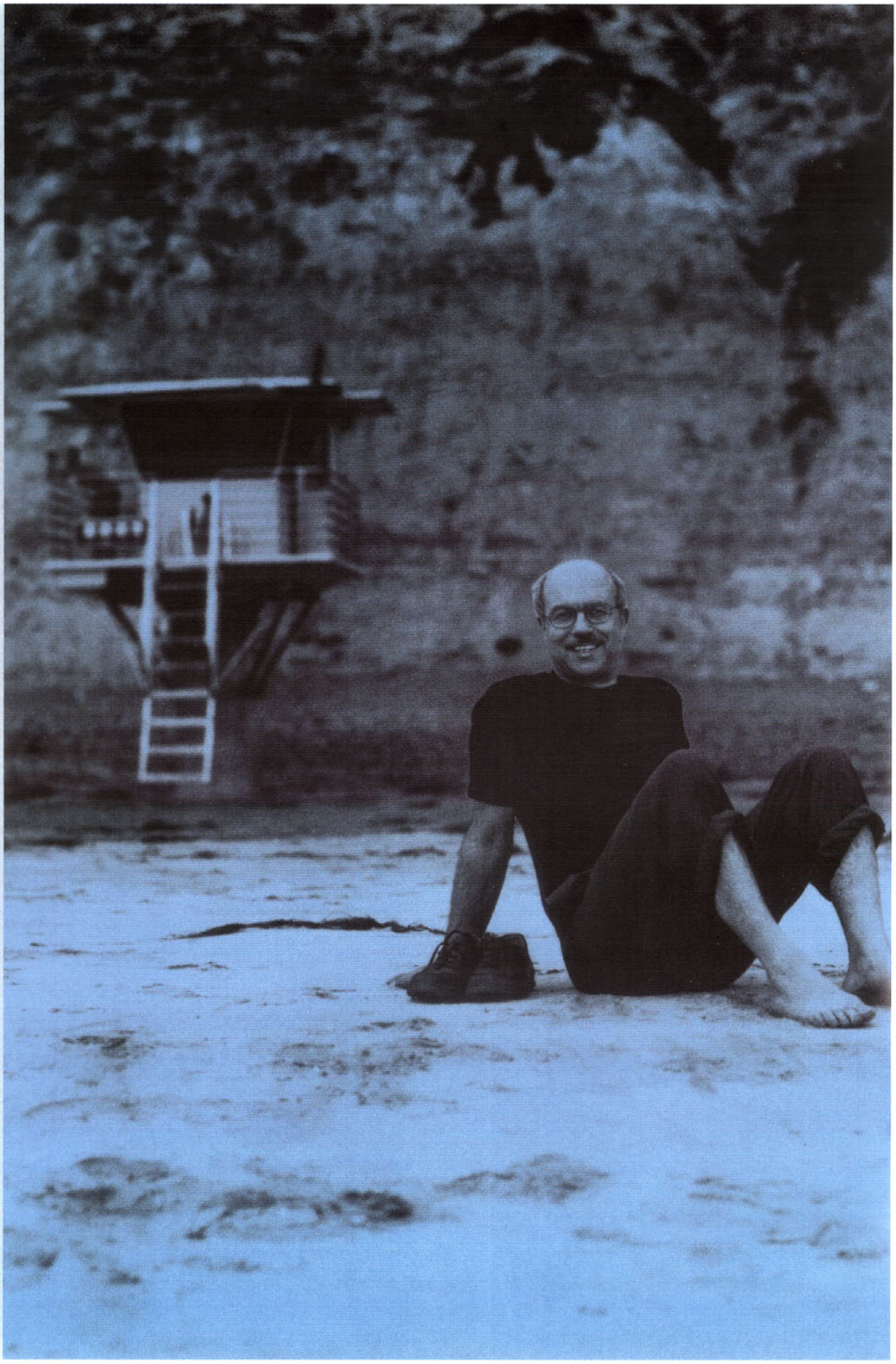

More than 500 scientific papers, two books, 64 patents and countless awards and honors – proof of a successful career that began more than 30 years ago. For moments of relaxation, K.C. Nicolaou has his favorite spot on the beach in California. He feels it offers a bit of the Mediterranean flair of his native country, Cyprus. Life far from the sea – unthinkable

of nature. "The way the atoms are connected to form rings, chains, centers of stereochemistry – things like that. We have to construct all the ring frameworks, all the bridges between the various atoms, and worry about all the sensitive functionalities in the molecule," he says. "It is as if you gave someone a diagram of the Parthenon, it would be difficult to replicate exactly, even today, despite all our technology."

Undaunted by the relative crudeness of his synthetic powers, Nicolaou revels in the wonders of his art. "Our objective is to make molecules as brilliantly and efficiently as possible with rational thinking. You start with simple materials. You don't cut corners by taking another natural product and adding something to it – that's semisynthesis, an often useful process in itself," he says. To Nicolaou, the art is in devising and executing a strategy that goes from simple compounds any chemist can buy to the synthesis of the complete target molecule. "It might take as many as 80 to 100 steps, but it sharpens the mind and character of the practitioner in the process," he says.

There's certainly no doubt about the sharpness of Nicolaou's mind. During his over thirty-year career, he has published more than 500 scientific papers and two books, filed 64 patents, delivered countless lectures, and received numerous awards and honors. In addition, he eagerly follows and encourages the careers of the more than 300 graduate and postdoctoral students he has mentored over the years, a testament to the sharpness of his character.

Perhaps, too, his yearly trips to visit family and friends in Greece and Cyprus further nurture his soul. "When there, I feel like a different person. It brings me back to earth, makes me feel more relaxed," says Nicolaou, who has in the meantime become a U.S. citizen but regards himself as a citizen of the world with a high dose of Greek and European culture. "You need to become like Zorba the Greek once in a while. The music, the culture, the people – it is rejuvenating. I get some of that same feeling when I walk on the beach in California."

The fact that the neighboring cities of San Diego and La Jolla are right on the Pacific Ocean has not escaped Nicolaou's notice. Indeed, it is a primary reason he considers this region of California his second home. "I was born next to the sea. It's in my blood. I don't think I could live far from the sea," he says. The Mediterranean-like landscape of the area and frequent long walks on the beach bring relaxation and balance to his life, he reports.

From his reflections has emerged a personal philosophy about the role of the synthetic chemist. "Our objective is not necessarily to develop a new drug or to enable its mass production, even though these are welcome benefits of our research. Rather, it is to face the academic challenge of total synthesis with an open mind – to learn and design, discovering new science in the process." And he adds: "I feel that the most important mission of us academicians is to carry out basic research and educate young people, both of which facilitate the useful applications of our work by the industrial sector."

K. C. Nicolaou compares his scientific pursuits to Odysseus, who endured a ten-year journey back home, and in the end, acquired much wisdom from the challenges he had to overcome. "That's what it's like in our field. Indeed, the molecule that took us the longest time to conquer was brevetoxin B. That 12-year odyssey was more difficult than any of our previous endeavors," he says. "But reaching the target is not necessarily the most significant outcome of a total synthesis; it is the discoveries and inventions made along the way that count the most."

Jennifer Porro

Schering AG has confidence in the potential of nature

Humankind has exploited the healing powers of nature since ancient times, and this is still true today. The pharmaceutical industry gains many ideas for new active ingredients from nature – whether for immune suppression, antibiotics, hormone therapies or cytostatics. The use of natural substances also has a long tradition at Schering AG and began already in the 1920s. Today, products of the fertility control and hormone therapy research fields are based, for example, on natural steroids once obtained from barbasco roots.

Dr. Rainer Metternich, head of medical chemistry at Schering AG, is enthusiastic about the high innovative potential of natural products. "With scientists constantly finding new molecules with new structures in nature, our biological knowledge is also expanding."

And this has spurred the race to find cancer therapies. In addition to taxol, many other promising anticancer agents stem from nature. K. C. Nicolaou has developed suitable methods to synthesize a number of these substances.

The Artist with Atoms

For Kyriacos C. Nicolaou the synthesis of natural products is a creative process

Fortunate indeed are the human beings who earn a living by happily pursuing their life's passion. Work for them is not drudgery or a simple paycheck, but an opportunity to challenge the intellect, expand one's horizons, or create wonderful things. Like many scientists, Kyriacos C. ("K. C.") Nicolaou, Ph.D., the recipient of the Ernst Schering Prize for 2001, is so blessed. Probably best known for his total synthesis of taxol, a groundbreaking anticancer drug, Nicolaou is a recognized pioneer and leader in the field of total synthesis of natural products, and has synthesized a wide range of nature's most complex molecules and created a myriad of others.

Perhaps it is his Greek origins that give him such a zest for his work. Born in 1946 of Greek parents in a village on Cyprus that is now under Turkish occupation, Nicolaou and his family moved to London in the 1960s. He studied chemistry at the University of London, obtaining a B.Sc. and then a Ph.D. in 1972, did postdoctoral work at Columbia and Harvard, and became a professor at the University of Pennsylvania in 1976. Since 1989, he has held joint appointments as the Darlene Shiley Professor of Chemistry, the Chairman of the Chemistry Department and the Aline W. and L. S. Skaggs Professor of Chemical Biology at The Scripps Research Institute (La Jolla, California) and Professor of Chemistry at the University of California at San Diego.

The wide windows of his attractive modern offices at Scripps overlook a grove of eucalyptus and torrey pine trees and the nearby Pacific Ocean. Greek art and artifacts decorate the room and hallways. Books about the Ancient World are scattered about. "My heritage makes me very proud," says Nicolaou, when asked about the décor. "The ancient Greeks left us an invaluable legacy. They taught us how to ask questions about nature and how to go about answering them through analytical and creative thinking. They laid the foundation for the arts and sciences."

Nicolaou often uses the words "art" and "science" in the same breath, especially when discussing his great passion, the total synthesis of organic molecules. "There is artistry in the science of total synthesis," says Nicolaou, who views each plan to construct a molecule as a sequence of steps not unlike the notes of a musician, the moves of a ballet dancer, or the words of a poet. "Our science is limitlessly creative," he continues, "because nature gives us all these elements that we can combine into many shapes and forms using nature's laws and our imagination. There are endless possibilities because nature has designed molecules that chemists never could have dreamed of, each one teaching us something new and challenging us to replicate it and go beyond it at the same time."

The science of organic synthesis began with the medicinal use of natural products, reports Nicolaou. From at least Egyptian times, humans were collecting herbs and developing remedies for certain ailments. They had no idea what the active ingredients were, but nowadays, modern science can tell us. In fact, many of today's drugs, ranging from aspirin to anticancer medications, stem from natural sources.

In 1994 Nicolaou's team was among the first to synthesize taxol in a laboratory. Organic chemists had been working on a laboratory synthesis of this complex molecule for more than twenty years. The successful syntheses of the epothilones A and B (1996), eleutherobin and sarcodictyin A (both in 1997) are further milestones in the history of K. C. Nicolaou's laboratory at the The Scripps Research Institute.

"Our science is immensely creative"

The hunt for nature's compounds continues to this day, says Nicolaou, with scientists actively collecting bacteria, fungi, roots, leaves, flowers, bark and sea life around the world looking for new therapeutic compounds. "The ocean is virtually untapped – soft corals, sponges, anything living in the sea. We are only just beginning to examine those substances," he says.

The first true synthesizer of an organic product was German chemist Friedrich Wöhler, who, in 1828, serendipitously created urea from an inorganic substance. "Since that time," says Nicolaou, "the art has been advancing, so that today we can synthesize very complex structures in the laboratory. However, our efficiency still needs to be improved. We are far from the power that nature has in this regard." In fact, Nicolaou puts the power of today's synthetic chemists in the Stone Age compared with that

The natural products of the sea are still largely unexplored. But substances from a particular species of coral look promising for medical application. Eleutherobin and sarcodictyin, for example, are considered potential anticancer agents. K. C. Nicolaou has developed ways to synthesize these compounds in the laboratory – so the coral remains untouched