

Midsummer madness

How an unexpected allegory led to the birth of a new subject.

Gautam R. Desiraju

I have always regarded myself as unconventional, taking roads not taken by others. Therefore, in 1978, despite a green card and being armed with a PhD from the University of Illinois, I came home permanently to India. Everyone else I knew was travelling in the opposite direction.

Of course, my idealism had wings of wax, which began to melt in the enervating heat and dust of the fledgling University of Hyderabad. The infrastructure in our labs was abysmal and, literally, state-of-the-ark. There was no sign whatsoever of a single crystal X-ray diffractometer, the main equipment that I needed for my work on crystal structure determination. We operated out of what were little more than sheds. In addition, the scientific system was charmingly rural, and I did not want to understand it. The organic solid-state chemistry I had learnt in the United States seemed better related to life on another planet. I knew I had to visit a laboratory abroad before I began to abandon hope.

The summer of 1982 found me in Cambridge where John Meurig Thomas had just begun a vigorous programme on organic topotactic reactions, in which solid reactants transform to products without loss of crystallinity. I was not prepared for what I would encounter. The Thomas group was large and purposeful, but tackled all their problems in a seemingly relaxed manner. Then there was Cambridge itself, with its restful colleges serenely silhouetted against the mild magic of an English summer. The long days and short nights, with the sky refusing to darken into the familiar ink-black of the tropics, only heightened my exhilaration and anxiety. I worked on topotactic reactions with a sinking feeling. With no equipment back at home, I knew I would soon be reduced to a guest worker in Cambridge. Still, I returned to Cambridge the following summer, but this time my predilection for the unconventional lured me into the company of Simon Kearsley and Noel Thomas — the maverick students of the group — who were working on problems largely unconnected with topotaxy.

Simon and Noel were looking at crystal structures just to see if they could understand

why they were packed the way that they were. But back then, this was not really a topic fit for research. Determining the structure of a crystal was difficult enough; few people worried about how different crystal structures interrelated — it was simply too difficult, and not enough was known. Aleksander I. Kitaigorodskii had said that close-packing of molecules was all that mattered, with this close-packing resulting in low crystal symmetry. Gerhard Schmidt, on the other hand, had tried to ‘engineer’ crystal structures by molecular manipulation. His so-called



Crystal-gazing: a placement at Cambridge had an unexpected influence.

‘chloro rule’ stated that planar aromatic molecules with two chloro-group substitutions tend to form crystals with a short axis of 4.0 Å. This was all that was known about the packing systematics of organic compounds.

Simon, Noel and I were not even housed with the rest of the group. We occupied a cavernous undergraduate laboratory that lay deserted for those summer months, save for hundreds of models — papier mâché lions, huge wooden cannonballs and metal wire storks sent in by ‘A’-level students from across the world for their practical examinations. The room was piled high with these curiosities and they stared eerily at us during the long evening hours, as we in turn stared at crystal structures. Fortuitously, the Cambridge Structural Database (CSD) was being developed by Olga Kennard and her associates in the very same building at the time, so Simon and Noel were able to retrieve crystal structures using this brand new computational tool.

The turning point in my research came when Noel showed me the crystal structures of the six isomeric dichlorophenols that he had extracted from the CSD to verify

Schmidt’s chloro rule. We noticed something rather unusual. Only three of the compounds obeyed the rule, but these were the three that crystallized with higher symmetries, violating Kitaigorodskii’s rule. The three other isomers did exactly the opposite. They did not have 4 Å axes, but they adopted low-symmetry space groups. So, either Schmidt or Kitaigorodskii was correct, but not both, in any particular instance. This meant that violations of the close-packing principle could be rationalized on the basis of effects of specific groups and directional interactions. My excitement quickened when I realized that by studying these interactions, it might be possible to discern rules for designing organic solids with specific physical and chemical properties — the goal of ‘crystal engineering’. With 50,000 crystals in the CSD (and no prospect of a diffractometer back home!), surely crystal-gazing was going to be a sporting proposition. Of course, this all came much later, and we were happy enough to show our results to John Meurig Thomas who generously suggested that Noel and I publish this work independently.

Our observations that day radically altered the way I looked at science and the directions my research took thereafter. Since then, the work I have done has had a major impact on the growth and development of crystal engineering, but much of it goes back to that single result and its implications. Today, when crystal engineering is described as “one of the principal challenges of modern chemistry” (*Chem Eur. J.* **10**, 3783–3791, 2004), I recall with amusement the irreverence with which Simon, Noel and I would discuss crystal packing. It was probably our midsummer madness that made us question existing concepts and paradigms. Without quite realizing it, we were supervising the birth of a new subject. ■

Gautam R. Desiraju is in the School of Chemistry, University of Hyderabad, Hyderabad 500 046, India.

FURTHER READING

Desiraju, G. R. *Crystal Engineering* (Elsevier, Amsterdam, 1989)

Desiraju, G. R. *Angew. Chem. Int. Ed. Engl.* **34**, 2311–2327 (1995).

Desiraju, G. R. & Steiner, T. *The Weak Hydrogen Bond in Structural Chemistry and Biology* (Oxford Univ. Press, Oxford, 1999).