

Gautam R. Desiraju

School of Chemistry, University of Hyderabad, Hyderabad 500 046, India.
E-mail: desiraju@uohyd.ernet.in

Received 27th October 2003, Accepted 4th November 2003

First published as an Advance Article on the web 13th November 2003

Problems with nomenclature are necessary evils in the development of a new subject. As the subject of crystal engineering progresses, it is possible and indeed advantageous to assess terminology, keep what is good, and discard what is not required. Names are coined easily in the early days of a subject. This arises partly from enthusiasm and partly because it is difficult to describe new concepts with old names. Or so we seem to feel. As crystal engineering has evolved into a more mature discipline, one also realizes that some of the terms that we used during the last 15 years or so in describing crystals and their design and properties might not have been really necessary and that standard terminology in the existing chemical and crystallographic literature might well have sufficed. More particularly, I refer to the term *co-crystal* (also written as *cocrystal*).

I do not know exactly when this term came into the literature. Perhaps it was in the paper of Etter and Panunto on the complexing ability of 1,3-bis(*m*-nitrophenyl)urea.¹ Whatever the case, the term gained easy acceptance. The operational word here is 'easy'. Anyone could understand that a co-crystal was what one got in a co-crystallization experiment, and gradually the term came to be used for just about any two- and higher-component crystal. At this point, it would do one good to remember that we had (and still have) a perfectly good word to describe multi-component crystals, which have specific non-covalent interactions between the distinct molecules, and this is *molecular complex*.² For someone whose serious early chemical education included the study of Foster's book³ on donor-acceptor complexes and Herbstein's illuminating work in this area⁴ (for those too young to know or care, my Ph.D. topic was in the area of quinone-hydroquinone donor acceptor complexes), the term *molecular complex* was perfectly acceptable and I have used it invariably in my papers. Recently, however, the term *co-crystal* slipped into a paper (that too in the title) where I was not the corresponding author⁵ and this has prompted the present letter.

I was always uncomfortable with the term *co-crystal* but not in ways I could express satisfactorily. For a start, the word *crystal* is too important, too meaningful and too evocative.⁶ For those in the subject of crystal engineering, it is a sacrosanct word—something like *bond* to a chemist. Given the centrality of the concept of a crystal, what is a *co-crystal*? I never had any problems with *co-crystallization* or *co-crystallize* and indeed I use these terms regularly. It was the simple, easy word *co-crystal* that caused me problems. Now, a crystal is described both by a lattice, which gives us the symmetry information, and also by the atoms/ions/molecules that are contained in it, the chemical information. So how can something like 1:1 1,3-bis(*m*-nitrophenyl)urea-triphenylphosphine oxide masquerade as a co-crystal, when it has nothing in common with the crystal of either 1,3-bis(*m*-nitrophenyl)urea or that of triphenylphosphine oxide? What is co- to what? In the end, would brass become a co-crystal of copper and zinc? Or are my questions too naive?

It was Herbstein again who, through his recent paper on composite crystals of 5-oxatricyclo[5.1.0.0^{1,3}]octan-4-one,⁷

resolved my nebulous doubts and brought my objections to the present use of the term *co-crystal* into sharper focus. He defines a *composite crystal* as something that is formed by 'ordered agglutination of crystals of the same or different type'. He is speaking literally about two different crystals stuck together at the molecular level. This to my mind is a real co-crystal—two crystals that are joined together. In his paper written 40 years ago on hexabromobenzene, he provides us with another beautiful example of a composite crystal.⁸ Because this crystal is pseudo-hexagonal with $c/a \sim 1/\sqrt{3}$, planes like (101) and (10-1) or (301) and (001) coincide, but not exactly, and what one gets is a mosaic of crystals joined along these nearly common planes. In a recent authoritative work, Chapuis and his group discuss urotropin azelate.⁹ These authors actually call this an 'unwilling co-crystal' in their paper title because each of the components, urotropin and azelaiic acid, retain many of their original crystal traits in the conjunction of these substances. Now this is what I would call a good co-crystal because, once more, vestigial influences of former beings persist. However, so prevalent has the present connotation of the term *co-crystal* become that something that is a really good example of a co-crystal is referred to in almost exactly the opposite terms! The Chapuis group have another paper on the σ -structure of β -tantalum, and here the composite portions of a true co-crystal have different space groups.¹⁰ This is not all. Alivisatos and co-workers have recently shown how a nanocrystal tetrapod of CdTe grows.¹¹ When it nucleates, it starts off as a cubic phase and when it branches out it switches to a hexagonal phase. Two crystals living together—I'd call this a co-crystal for sure. I will round off this selection of examples with Boese's fascinating studies of what he calls oligodiffractometry.¹² Here we have crystals of polymorphs that are necessarily examined together in the diffraction experiment and their patterns deconvoluted later—a different type of co-crystal maybe but still a co-crystal. In none of these cases, however, has my image of a crystal been dimmed and yet we have two or more crystals somehow connected with each other intimately.

So what do we do with the 1:1 1,3-bis(*m*-nitrophenyl)urea-triphenylphosphine oxide co-crystal? For a start, I'd revert to calling it the 1:1 1,3-bis(*m*-nitrophenyl)urea-triphenylphosphine oxide molecular complex. This is a good term and a clear one at that. It tells us what is happening, and it is general enough. It may be distinguished from the terms *solid solution* or *inclusion compound* and the reader who is further interested in all these terminologies is well advised to read Kitaigorodskii's book.²

To conclude, when new terms enter the literature in a big way, and there is some controversy regarding their use, I would suggest that there are two possible courses of action. If the term is merely ambiguous, it may be easiest to just retain it because it has become too common. A good example of this situation is the use of the term *pseudopolymorph*.¹³ But if something is scientifically suspect it must go, howsoever popular it might be. What is easy is sometimes not what is best.

References

- 1 M. C. Etter and T. W. Panunto, *J. Am. Chem. Soc.*, 1988, **110**, 5896.
- 2 A. I. Kitaigorodskii, *Mixed Crystals*, Springer, Berlin, 1984, p. 275.
- 3 R. Foster, *Organic Charge-Transfer Complexes*, Academic Press, New York, 1969.
- 4 F. H. Herbstein, in *Perspectives in Structural Chemistry*, ed. J. D. Dunitz and J. A. Ibers, vol. IV, pp. 166–394, 1971.
- 5 J. Zyss, I. Ledoux-Rak, H. -C. Weiss, D. Bläser, R. Boese, P. K. Thallapally, V. R. Thalladi and G. R. Desiraju, *Chem. Mater.*, 2003, **15**, 3063.
- 6 G. R. Desiraju, *Nature (London)*, 2003, **423**, 485.
- 7 F. H. Herbstein, *Acta Crystallogr., Sect. B*, 2003, **59**, 303.
- 8 E. G. Boonstra and F. H. Herbstein, *Acta Crystallogr.*, 1963, **16**, 252.
- 9 M. Bonin, T. R. Welberry, M. Hostettler, M. Gardon, H. Birkedal, G. Chapuis, P. Mockli, C. A. Ogle and K. J. Schenk, *Acta Crystallogr., Sect. B*, 2003, **59**, 72.
- 10 A. Arakcheeva, G. Chapuis, H. Birkedal, P. Pattison and V. Grinevitch, *Acta Crystallogr., Sect. B*, 2003, **59**, 324.
- 11 L. Manna, D. J. Milliron, A. Meisel, E. C. Scher and A. P. Alivisatos, *Nat. Mater.*, 2003, **2**, 382.
- 12 R. Boese, M. T. Kirchner, W. E. Billups and L. R. Norman, *Angew. Chem. Int. Ed.*, 2003, **42**, 1961.
- 13 R. K. R. Jetti, R. Boese, P. K. Thallapally and G. R. Desiraju, *Cryst. Growth Des. ASAP*.