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Attrition-induced deracemization of racemizable crystal-liquid suspensions for the production of industrially relevant compounds

It has been demonstrated that certain chiral racemic compounds sensitive to catalyzed racemization in solution, when subjected to strong grinding as suspensions, deracemize entirely. A strict additional requirement is that the compounds should be conglomerates. How does this happen? It is thought that relatively rare primary nucleation of the racemic conglomerate provides a crystal that must have single handedness. Rapid secondary nucleation under conditions whereby growing crystals are continuously shattered leads to rapid propagation of that handedness. The process resembles closely to Ostwald ripening. The direction of deracemization can be determined by addition of a small amount of enantiomerically pure seed crystal. This process has been used to generate single enantiomers of commercially interesting compounds such as naproxen, clopidogrel and prasugrel. Various extensions of this methodology have been developed and also methods for scale up have been developed both by us and by others.

Biography

Richard M Kellogg was Professor of Chemistry at the University of Groningen, Netherlands for 25 years. He co-founded the contract research organization Syncom BV for which he is still a Scientific Advisor. He is also Chief Scientific Officer of Philae Pharmaceuticals; a company devoted the use of RNA technology for the treatment of skin diseases.

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