Assigning the absolute configuration of liquid chiral molecules by capillary crystallization

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Asymmetric catalysis is an important and continuously growing field in chemical science. Reaction products include small chiral molecules, which are often liquid at ambient conditions.

Obtaining suitable single crystals for X-ray diffraction is a limiting factor for structural investigations of molecular compounds. In several cases, the conventional crystallization methods e.g. solvent evaporation, sublimation, etc. are not able to deliver suitable crystals. If the compound is liquid under ambient conditions, such techniques are not applicable. Resourceful developments occurred over 70 years ago, as Fankuchen et al. first reported the crystallization of a liquid compound in a capillary surrounded by a cold gas stream.[1] In the meantime, a manifold of improvements have been made to apply this simple and powerful method to a variety of different compounds including gases.[2-4]

It is worth noting, that to the best of our knowledge, the capillary crystallization has not been used for absolute configuration assignment so far. Based on the observation that the absolute structure parameter could be accurately assigned for an achiral molecule (2-Methylfuran, Ref.code: ZOGQUK) in a non-centrosymmetric space group we asked ourselves, whether it is possible to determine the absolute configuration of an enantiopure liquid.[5] Since then we have demonstrated this for some selected examples including reaction products, natural products as well as flavoring agents containing only light atoms (C, H, N, O).[6-7]

The main advantages of the method are that only a small sample amount (~5 mg) is required and that there is no need to rely on reference substances to determine the absolute configuration. Moreover, the capillary crystallization is a non-destructive method. During the experimental studies, we observed two main limitations for the capillary crystallization, such as solid-solid phase transitions at low temperatures and formation of amorphous glassy phases.

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