Versatile methods for promoting crystallinity in small molecules

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While the contemporary focus of organic research has shifted from synthesis of specific molecules to production of desirable properties,[1] crystallinity of chemicals has attracted much attention, as it replaces solvent-intensive column chromatography with recrystallization,[2] enables characterization *via* X-ray crystallography, and participates in asymmetric catalysis through diastereoconvergent crystallizations.[3,4] Therefore, it would be promising to propose versatile methods for effectively promoting crystallinity of small, non-crystalline molecules. Herein we report two separate methods of promoting on-demand crystallinity:

Semicarbazones are a class of chemicals exhibiting crystallinity and stability under most reaction conditions,[5] so a strategy of incorporating semicarbazone subunits to target molecules without affecting original reactivity would be desirable in enhancing product crystallinity. Therefore, by designing a cheap, two-step synthesis of alkynyl semicarbazones and attaching azido groups onto esters, we successfully connected semicarbazone subunits to a wide range of esters *via* copper-catalyzed azide-alkyne cycloadditions (CuAACs) and greatly enhanced the crystallinity of esters *via* melting point analysis.

For other small molecules being unable to perform CuAAC, another approach to enhancing crystallinity is to form co-crystallization complexes with large molecules. Therefore, we successfully designed three tetraaryladamantanes (TAAs), a class of compounds that have been reported as co-crystallization chaperones for various common chemical feedstocks.[6,7]

References

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