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Crystallization in Capillary Spaces: Preparation and Characterization of a Novel, High-Energy Polymorph of Nabumetone

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Abstract

Data from SSCI laboratories show that 85% of compounds which are subjected to polymorph screening can be isolated in multiple solid forms. The generation of seeds of high free energy crystalline forms often requires special conditions. One such condition is crystallization from solution in capillary spaces, which allows high supersaturation to be attained in a quiescent environment. A demonstration of the power of this technique in generation of high free energy crystal forms is the discovery of a new polymorph of nabumetone (4-(6-methoxy-2-naphthalenyl)-2-butanone). The new form (form II) was crystallized in capillaries from a variety of solvents and was characterized by x-ray powder diffraction, single crystal x-ray analysis, and hot-stage microscopy. Form II is metastable, readily converting to the known form I under minimal mechanical stress. It has proven difficult to crystallize and isolate nabumetone form II using standard techniques because of its sensitivity to mechanical stress. However, new forms of other compounds which are stable and can be isolated using standard techniques have also been generated by capillary crystallization.