Utility of the Ammonia-Free Birch Reduction of Electron-Deficient Pyrroles: Total Synthesis of the 20S Proteasome Inhibitor, *clasto*-Lactacystin β-Lactone

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Abstract
A new synthesis of the 20S proteasome inhibitor *clasto*-lactacystin β-lactone is described. Our route to this important natural product involves the partial reduction of an electron deficient pyrrole as a key step. By judicious choice of enolate counterion, we were able to exert complete control over the stereoselectivity of the reduction/aldol reaction. Early attempts to complete the synthesis by using a C-4 methyl substituted pyrrole are described in full, together with our attempts to promote regioselective elimination of a tertiary alcohol. The lessons learnt from this first approach led us to develop another, and ultimately successful, route that introduced the C-4 methyl group at a late stage in the synthesis. Our successful route is then described and this contains several highly stereoselective steps including a *cis*-dihydroxylation and an enolate methylation. The final synthesis proceeds in just 13 steps and in 15 % overall yield making it an extremely efficient route to this valuable compound.