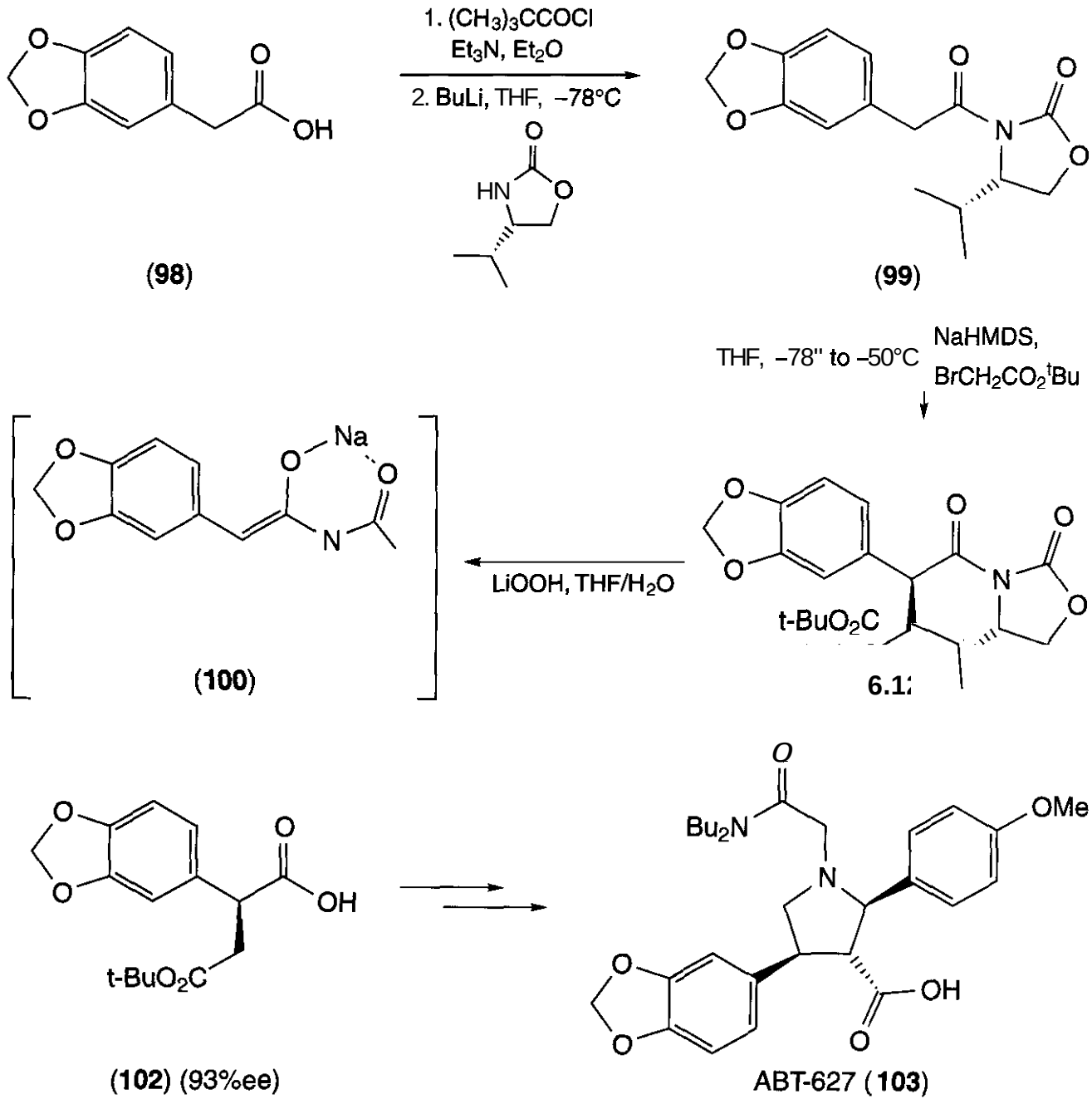

Figure 18.39.

iary is then removed (and preferably recovered), providing the product in high enantiomeric excess. This process is most attractive when both isomers of the auxiliary are readily available in enantiomerically pure form, and where the reaction leads to high levels of stereoselectivity in a predictable manner. Attaching and removing the auxiliary should be straightforward and proceed without loss of stereochemical integrity.

Many auxiliaries currently in use are derived from 1,2-amino alcohols (140). These are readily available from natural sources with little or no synthetic manipulation and can react in a variety of ways to form conformationally well-defined (usually cyclic) auxiliary systems. The use of oxazolidinones in asymmetric synthesis was developed by Evans et al., and these oxazolidinones have been used extensivelvin a variety of different reactions (140, 141). The use of this chiral auxiliary in the preparation of pharmaceuticals is widespread, and there are several large-scale processes using such chemistry (142).

Abbott reported an improved synthesis of ABT-627 (98)involving an asymmetric alkylation of the valine-derived acyl oxazolidinone (99) (143). ABT-627 (Atrasentan) is a selective endothelin ET_A receptor antagonist under development for the treatment of cancer, particularly prostrate cancer. Acid (100) was activated as a mixed anhydride and treated with the lithium anion of the oxazolidinone to give (101). Both of the following deprotonation and alkylation steps must be controlled to give high levels of stereoselectivity. The (Z)-enolate (102) is favored, both kinetically and thermodynamically, by the bulky iso-propyl group