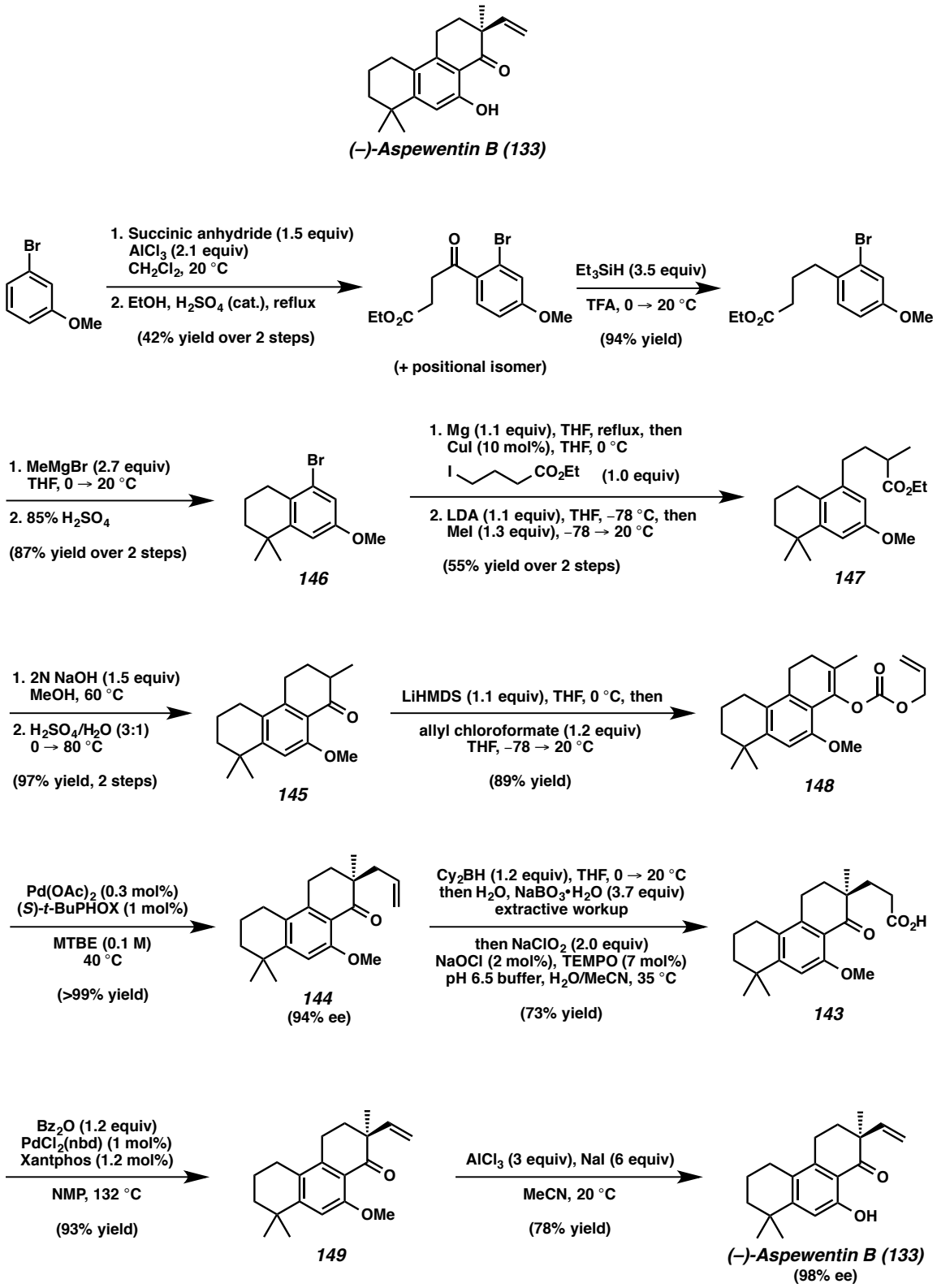
APPENDIX 9

Synthetic Route for (–)-Aspewentin B


(–)-Aspewentin B (133)
1. Succinic anhydride (1.5 equiv)
AlCl3 (2.1 equiv)
CH2Cl2, 20 °C
2. EtOH, H2SO4 (cat.), reflux
(42% yield over 2 steps)
(+ positional isomer)
Et3SiH (3.5 equiv)
TFA, 0 → 20 °C
(94% yield)
1. MeMgBr (2.7 equiv)
THF, 0 → 20 °C
2. 85% H2SO4
(87% yield over 2 steps)
146
1. Mg (1.1 equiv), THF, reflux, then
CuI (10 mol%), THF, 0 °C
(1.0 equiv)
2. LDA (1.1 equiv), THF, –78 °C, then
MeI (1.3 equiv), –78 → 20 °C
(55% yield over 2 steps)
147
1. 2N NaOH (1.5 equiv)
MeOH, 60 °C
2. H2SO4/H2O (3:1)
0 → 80 °C
(97% yield, 2 steps)
145
LiHMDS (1.1 equiv), THF, 0 °C, then
allyl chloroformate (1.2 equiv)
THF, –78 → 20 °C
(89% yield)
148
Pd(OAc)2 (0.3 mol%)
(S)-t-BuPHOX (1 mol%)
MTBE (0.1 M)
40 °C
(>99% yield)
144
(94% ee)
Cy2BH (1.2 equiv), THF, 0 → 20 °C
then H2O, NaBO3•H2O (3.7 equiv)
extractive workup
then NaClO2 (2.0 equiv)
NaOCl (2 mol%), TEMPO (7 mol%)
pH 6.5 buffer, H2O/MeCN, 35 °C
(73% yield)
143
Bz2O (1.2 equiv)
PdCl2(nbd) (1 mol%)
Xantphos (1.2 mol%)
NMP, 132 °C
(93% yield)
149
AlCl3 (3 equiv), NaI (6 equiv)
MeCN, 20 °C
(78% yield)
(–)-Aspewentin B (133)
(98% ee)