Total Synthesis and Structure Revision of (+)-Lancilactone C Domino [4+3] cycloaddition Hidetaka Kuroiwa, Soichiro Suzuki, Kazuhiro Irie, and Chihiro Tsukano* oxidation Cite this: J. Am. Chem. Soc. 2023, 145, 27, 14587-14591 - Diels-Alder - elimination unstable - 6π-electrocyclization Structure revision based on NMR, plausible biosynthesis and total synthesis instead of NH3 ene reaction d) TBSOTf, 2,6-lut. CH₂Cl₂, 0 °C, qua b) KOH, MeOH-H₂O 0 to 23 °C THE, 0 °C c) NaBH₄, NaOH EtOH-H₂O, 0 °C 35% (3 steps) e) EtPPh₃Br, tBuOK THF, reflux 70% (Z:E = 9:1) TBSÖ (-)-8 (99%ee) (+)-7 $\frac{(Z:E=9:1)}{+ S.M.}$ (three cycles) k) vinylMgBr, CeCl₃ THF, -78 °C, 78% f) AlMe₃, (CH₂O)_n DTBMP CH₂Cl₂, -50 °C 76%, dr >20:1 OTBDPS OTBDPS OH i) TBDPSCI, imid DMF, 40 °C dr >20:1 I) PCC, CH₂Cl₂, 83% g) H₂, Pd/C, ElOAc dr 4:1 h) TBAF, DMF, 90 °C i) TPAP, NMO MS 4 A, CH₂Cl₂ ö cat. pTsOH, 60 (+)-11 88% (2 steps) 3(E:Z=5:1)74% (2 steps) ÇO₂Et Dess-Martin periodinane CH2Cl2, 23 °C endo-anti selectivivty dr 1:1 ÒН EtO EtC E:Z = 5:1only (E)-3 (3R)-4was reacted. (90%ee) 12c 12d 1:1 matching electronic and steric factors then CSA a) MeMgBr, CeCl₃ THF, -78 °C c) DIBAL-H CH₂Cl₂, -78 °C d) (MeO)₂P(O)CH₂CO₂Me fBuOK, THF, -10 °C E:Z = 3:1 b) pTsOH·H2O CH₂Cl₂ 66% (2 steps) EtÓ e) NaBH₄, NICI₂·6H₂O MeOH, 42% (3 steps) (5R)-2c 50% (5R)-2d 12% (4.2:1)(undesired) (desired) g) TBAF, THF 45 °C, 97% h) AZADOL Phi(OAc)₂, CH₂Cl₂ f) pTsOH·H₂O 110 °C, 68% i) (+)-lpc₂allyibor THF, -78 °C 91% (2 steps) dr 11:1 (-)-14 (+)-15 Et₃N, DMAP CH₂Cl₂, 0 °C k) Hoveyda-Grubbs δ 6.91 (m) 2nd gen. cat. toluene, 70 °C H_c δ 6.79 (m) 61% (2 steps) I) Me₃SnOH CICH₂CH₂CI reflux, 67% Lancilactone C (1a) (reported data H_a δ 6.90 (s) H_b δ 6.76 (s) H_c δ 6.25 (s) (proposed structure) 1b (revised structure) g) NaBH₄ NiCl₂-6H₂O, MeOH h) Dess-Martin a) Comins' reagent KHMDS, 87% DIBAL-H d) toluene CH₂Cl₂, -78 °C 43% (3 steps) THF, -78 °C reflux peridodinane, CH₂Cl₂ b) 17, Pd(PPh₃)₄ Cs₂CO₃, THF-H₂O 65 °C, 57% c) 18, DMAP then DDQ f) Ph₃P=CHCO₂tBu tBuC toluene, 80 °C i) iPrPPh₃I, nBuLi THF, 0 to 23 °C (+)-19 (R = TBDPS) 81%, E:Z >20:1 82% (3 steps) OH (+)-21 ene, 62% l) (+)-lpc₂allylborane THF, -78 °C 72%, dr 10:1 m) methacrylic anhydride CHO

m) methacrylic ann DMAP, CH₂Cl₂

n) Hoveyda-Grubbs

2nd gen. cat. toluene, 80 °C 59% (2 steps) o) TMSOTf, 2,6-lut

CH₂Cl₂, 99%

(+)-23

17

18

+)-tancilactone C (1b) (revised sturucture)

j) TBAF, THF 50 °C, 99%

k) AZADOL

(+)-22

Phi(OAc)₂ CH₂Cl₂, 89%