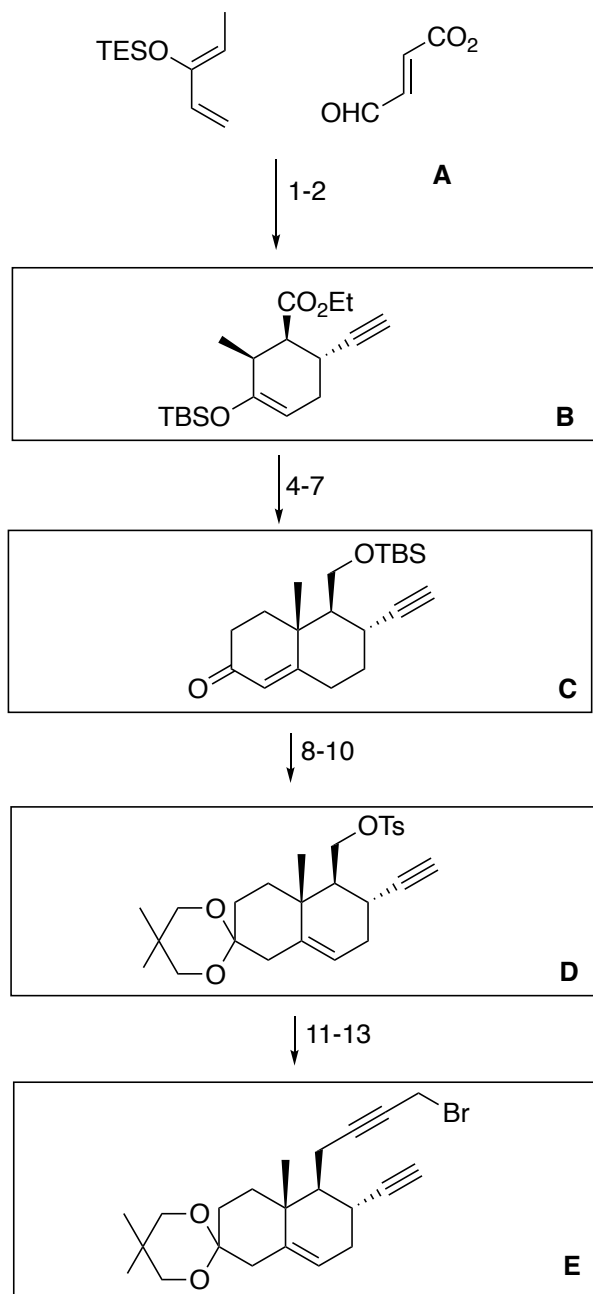


Synthesis Challenge 98

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<https://doi.org/10.1021/jacs.1c08756>
 06.10.2021

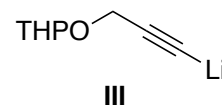
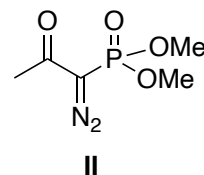
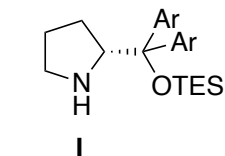


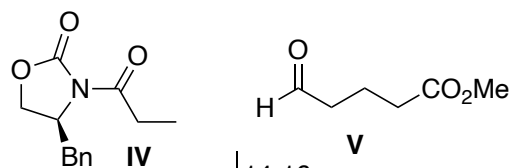
1) **I** (10 mol %), CF₃CO₂H (20 mol %), -10 °C, PhMe,
 2) KOEt (3.2 equiv), **II** (3.6 equiv), -78 °C, THF

3) DIBAL-H (3.3 equiv), -78 °C to rt, THF, 3 h then add MeOH (1.2 equiv), *n*-Bu₄NF (3 equiv), 0 °C
 4) TBSCl (1.1 equiv), imidazole (1.5 equiv), 4-DMAP (0.1 equiv), 0 °C to rt, CH₂Cl₂
 5) TMSI (1.2 equiv), HMDS (1.6 equiv),
 6) Methyl vinyl ketone (2 equiv), MeNO₂ (3 equiv), *i*-PrOH (3 equiv), BF₃·OEt₂ (2.3 equiv),
 7) NaOMe (1.6 equiv), rt to 40 °C, MeOH, 8 h

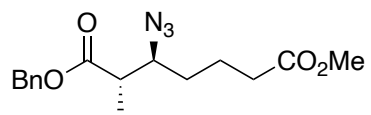
8) 2,2-Dimethylpropane-1,3-diol (5 equiv), PPTS (0.2 equiv), 100 °C, PhH,
 9) *n*-Bu₄NF (2 equiv), rt, THF
 10) *p*-TsCl (3 equiv), Et₃N (10 equiv), 4-DMAP (2 equiv), 0 °C to rt

11) Tetrahydro-2-(2-propynyloxy)-2H-pyran (2.5 equiv), *n*-BuLi (2.4 equiv), then add **III** (1 equiv)
 12) Bi(OTf)₃ (5 mol %), 2,2-Dimethylpropane-1,3-diol (5 equiv)
 13) CBr₄ (1.2 equiv), PPh₃ (1.5 equiv), *i*-Pr₂NEt

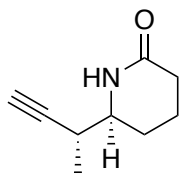




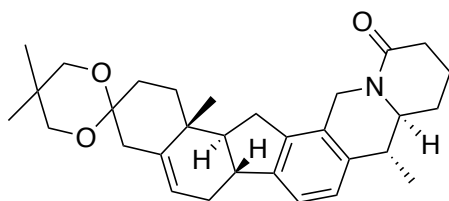
↓ 14-16



↓ 16-20



↓ 21-22



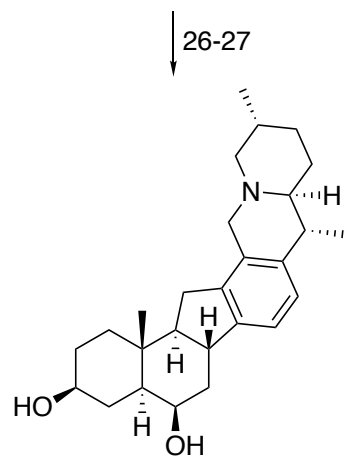
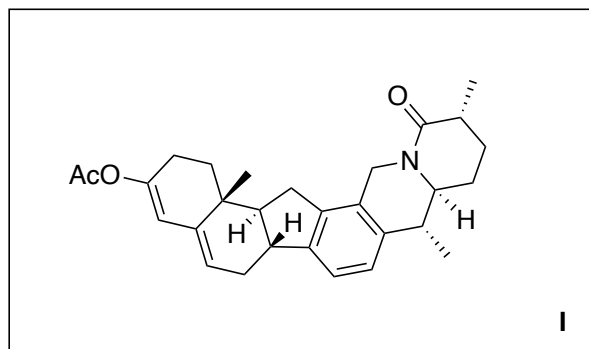
↓ 23-25

14) **IV** (1 equiv), *n*-Bu₂BOTf (1.1 equiv), *i*-Pr₂NEt (1.4 equiv), -78 to 0 °C, CH₂Cl₂, then add **V** (1.1 equiv), -78 °C to rt, then add MeOH/pH 7 buffer, 30% aq. H₂O₂
 15) PPh₃ (1.5 equiv), DIAD (1.5 equiv), DPPA (1.5 equiv), 0 °C to rt,
 16) Benzyl alcohol (2 equiv), *n*-BuLi (1.8 equiv), -78 to 0 °C, THF, 30 min, then -40 °C to -20 °C

17) PPh₃ (1.2 equiv), H₂O (10 equiv), 60 °C, THF
 18) LiBH₄ (5 equiv), MeOH (6 equiv), 0 °C to rt, THF
 19) Dess-Martin periodinane (1.3 equiv), rt, CH₂Cl₂, 3 h then add solid NaHCO₃
 20) KOEt (3.3 equiv), **II** (4 equiv)

21) **E** + **G** NaH (1.5 equiv), DMF, 0 °C to rt
 22) RhCl(PPh₃)₃ (10 mol %), EtOH, 80 °C

23) Lithium 2,2,6,6-tetramethylpiperidine (3 equiv), HMPA/THF (1:10), -78 °C, then add MeI (8 equiv), -78 °C, then add MeOH (quench), -78 °C
 24) *p*-TsOH·H₂O (2.5 equiv), H₂O, acetone, 0 °C to rt, 15 h (98%)
 25) TMSCl (4 equiv), NaI (4 equiv), Ac₂O, 0 °C,



26) *m*-CPBA (1.2 equiv), KH_2PO_4 - Na_2HPO_4 buffer (pH 8), 1,4-dioxane, 0 °C to rt
 27) HBr (0.1 equiv), Et_2O , rt, then add LiAlH_4 (3 equiv), -78 °C to rt, then add LiAlH_4 (4 equiv), rt to 60 °C