Asymmetric Total Synthesis and Structure Revision of (+)-Mangicol D

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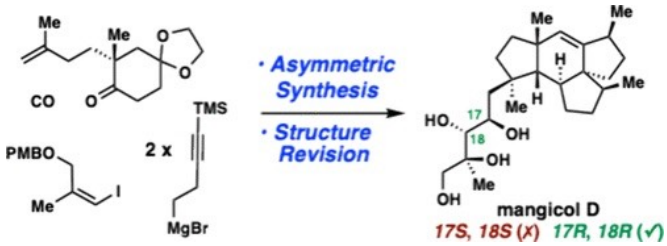
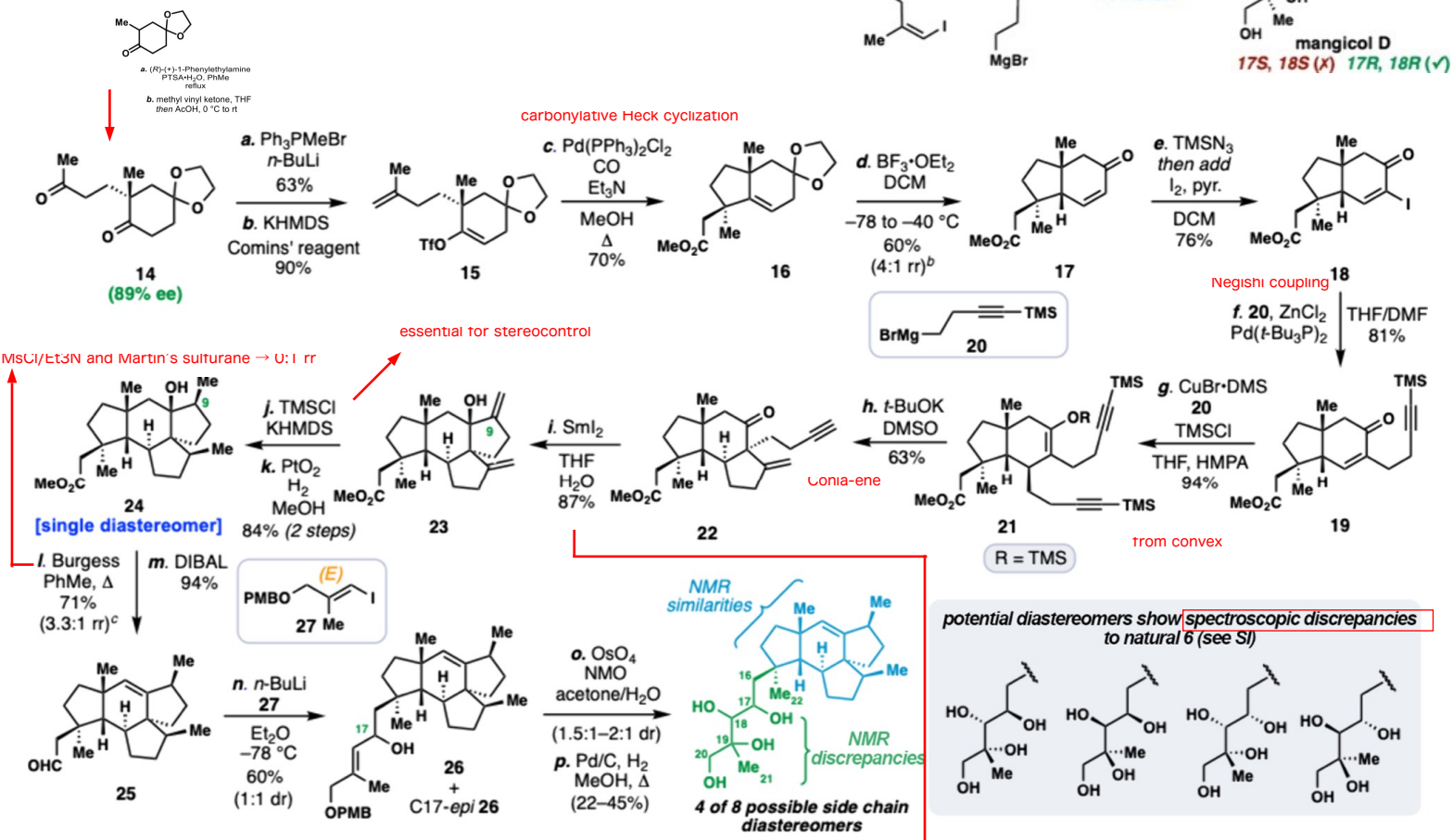
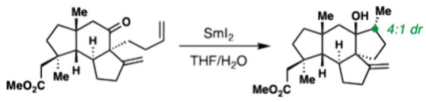
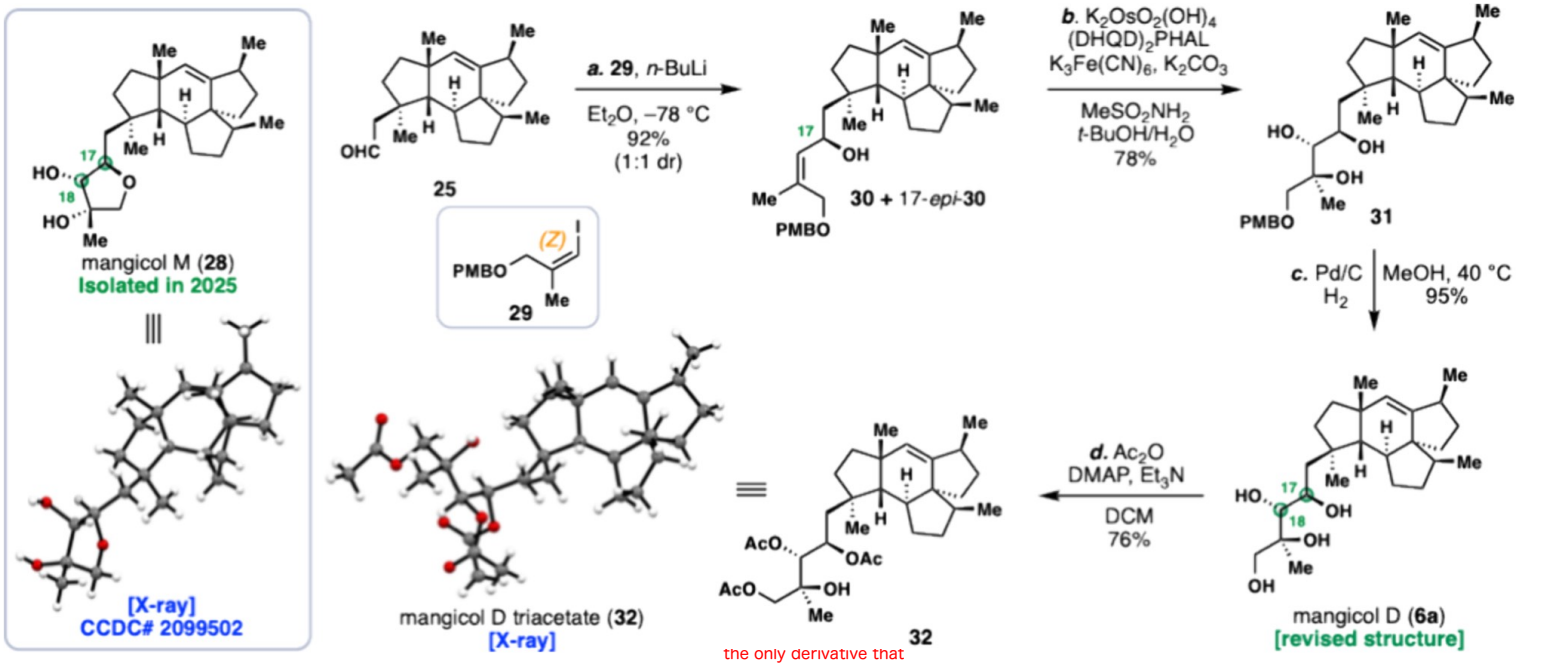




[a]Reagents and conditions: (a) Ph_3PMeBr (1.6 equiv), *n*-BuLi (1.5 equiv), THF, 0 °C, 2 h, 63%; (b) KHMDS (1.5 equiv), THF, −78 to 0 °C, 1.5 h, *then add* Comins' reagent (1.2 equiv), −78 °C, 1 h, 90%; (c) $Pd(PPh_3)_2Cl_2$ (0.05 equiv), Et_3N (1 equiv), CO balloon, MeOH, 60 °C, 2 h, 70%; (d) $BF_3{\cdot}OEt_2$ (30 equiv), DCM, −78 to −40 °C, 2 h, 60%; (e) $TMSN_3$ (2 equiv), DCM, 0 °C, 2 h, *then add* I_2 (2 equiv), pyridine, 0 to 23 °C, 24 h, 76%; (f) **20** (2 equiv), $ZnCl_2$ (2 equiv), THF, 0 °C, 30 min, *then add* **18**, $Pd(t\text{-}Bu_3P)_2$ (0.1 equiv), DMF, 0 to 23 °C, 2 h, 81%; (g) **20** (3 equiv), CuBr·DMS (1.5 equiv), THF, −78 °C, 30 min, *then add* **19**, TMSCl (2 equiv), HMPA (2 equiv), −78 °C, 30 min, 94%; (h) *t*-BuOK (0.75 equiv), DMSO, 23 °C, 30 min, 63%; (i) SmI_2 (8 equiv), THF, H_2O, 23 °C, 30 min, 87%; (j) TMSCl (6.5 equiv), KHMDS (6.5 equiv), THF, −78 °C, 1 h, 98%; (k) PtO_2 (0.1 equiv), H_2 balloon, MeOH, 23 °C, 24 h, 86%; (l) Burgess reagent (5 equiv), PhMe, 40 °C, 24 h, 71%; (m) DIBAL (1.1 equiv), DCM, −78 °C, 30 min, 94%; (n) **27** (2 equiv), *n*-BuLi (2 equiv), Et_2O, −78 °C, 20 min, *then add* **25**, −78 °C, 10 min, 60%, 1:1 *dr*; (o) OsO_4 (0.5 equiv), NMO (3 equiv), acetone, H_2O, 23 °C, 24 h, 1.5:1–2:1 *dr*; (p) Pd/C (20 wt.%), H_2 balloon, MeOH, 40 °C, 2 h, 22–45% over two steps (see SI). KHMDS = potassium bis(trimethylsilyl)amide, TMS = trimethylsilyl, DMS = dimethyl sulfide, HMPA = hexamethylphosphoramide, DIBAL = diisobutylaluminum hydride, PMB = *p*-methoxybenzyl. NMO = *N*-methylmorpholine *N*-oxide. [b]Minor isomer is the *β,γ*-unsaturated enone. [c]Minor isomer is the tetrasubstituted alkene.





[a]Reagents and conditions: (a) **29** (2 equiv), *n*-BuLi (2 equiv), Et_2O, −78 °C, 20 min, *then add* **25**, −78 °C, 10 min, 92%, 1:1 *dr*; (b) $K_2OsO_2(OH)_4$ (0.4 equiv), $(DHQD)_2PHAL$ (2 equiv), $K_3Fe(CN)_6$ (3 equiv), K_2CO_3 (3 equiv), $MeSO_2NH_2$ (1 equiv), *t*-BuOH, H_2O, 23 °C, 24 h, 78%; (c) Pd/C (20 wt.%), H_2 balloon, MeOH, 40 °C, 2 h, 95%; (d) Ac_2O (10 equiv), DMAP (10 equiv), Et_3N (10 equiv), DCM, 0 → 23 °C, 24 h, 76%. $(DHQD)_2PHAL$ = hydroquinidine 1,4-phthalazinediyl diether, DMAP = 4-dimethylaminopyridine.