Concise Enantioselective Total Synthesis of (+)-Punctaporonin U

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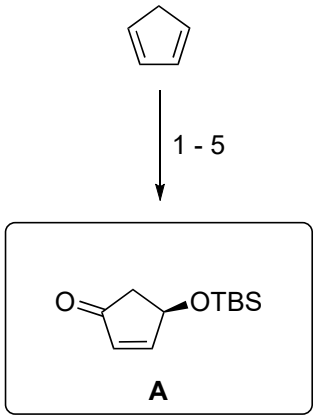
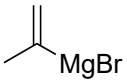
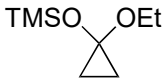


1) O_2, hν, Rose Bengal, Thiourea, MeOH
2) Vinyl acetate, Pancreatin lipase, NEt_3
3) TBSCl, Imidazole
4) K_2CO_3, MeOH
5) PCC



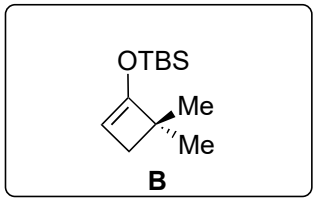
1

2) Racemic resolution. >99% ee

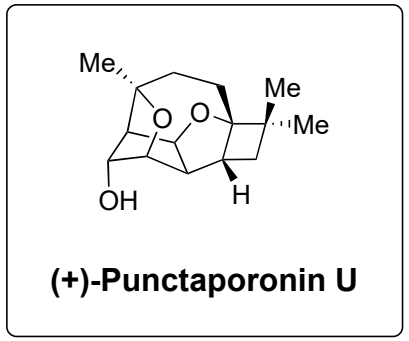


6 - 9

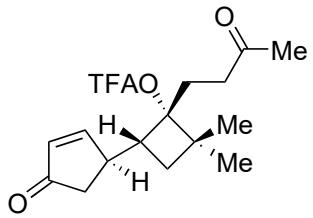
6) MeOH
7) MeMgBr, *then* **1**
8) 1 M HCl / Et_2O
9) KHMDS, TBSCl



8) Type of reaction?
Semi-pinacol rearrangement



10-12



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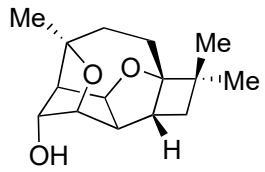
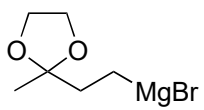
13-15

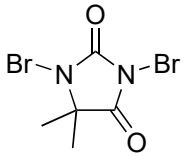


(+)-Punctaporonin U

10) **A**, **B** (2.0 equiv), TESOTf, (2,6-*t*Bu)pyridine, CH_2Cl_2, –40 °C
11) **2**, $LaCl_3 \cdot 2LiCl$
12) TFAA, pyridine, *then* $TsOH \cdot H_2O$



2



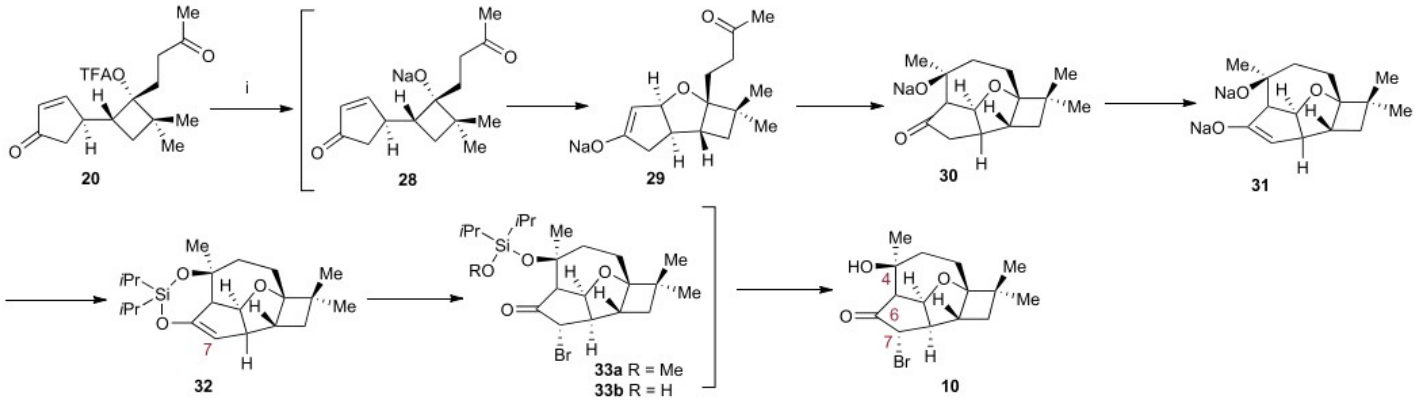
DBDMH

10) *Hint: syn* addition. dr 4:1. Name of reaction?
Mukaiyama-Michael

13) MeONa (2.5 equiv), *then* iPr_2SiCl_2, NEt_3, *then* DBDMH, *then* HF·pyridine. (50% yield)
14) $NMe_4BH(OAc)_3$
15) (2,6-*t*Bu)pyridine, 3 days

13) Draw a probable mechanism of the key step.
Hint: a dianion intermediate is formed
14) Name of reaction?
Evans Saksena anti-selective reduction

(b) Domino oxa-Michael/aldol/bromination sequence: A possible reaction pathway



[a]Reagents and conditions. (i) MeONa (2.5 equiv), DMF, −50 °C, 2 h then iPr_2SiCl_2 (4.0 equiv), Et_3N (3.0 equiv), −50 °C to rt, 30 min then DBDMH (0.7 equiv), −50 °C, 1 h then pyridine•$(HF)_x$ (150 equiv), −50 to 0 °C, 16 h, 50%; (ii) $NMe_4BH(OAc)_3$ (5.0 equiv), MeCN/AcOH (4:1), −20 to 0 °C, 6 h; (iii) 2,6-di-*tert*-butylpyridine (5.0 equiv), DMF, 65 °C, 72 h, 60% over two steps. DBDMH = 1,3-dibromo-5,5-dimethylhydantoin.