Total Synthesis of Lycoricidine and Narciclasine by Chemical Dearomatization of Bromobenzene

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- Lycoricidine, narciclasine are well-known anticancer agents, exhibiting submicromolar inhibitory activity against multiple cancer cell lines.

- These alkaloids possess a highly functionalized aminocyclitol core with four contiguous stereocenters.

- This work presented the total synthesis of lycoricidine and narciclasine based on a chemical based dearomatization of bromobenzenes as well as a general method for the preparation of 4-aryl-substituted cis-dihydrodiols.

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Synthesis Analysis

1. MTAD with visible light
   OsO₄, NMO, ArB(OH)₂
   → 5

2. Pd(dppf)Cl₂
   Et₃N, H₂O
   → 10a

3. 2,2-DMP
   PPTS
   → 12

4. KOH
   CuCl₂
   → 13

5. OH
   PIFA then TFA
   → 1

6. OH
   TBAF
   → 15

7. ArN=O then Zn, AcOH
   → 11a’

8. TIPSOTf
   2,6-lutidine
   → 17

9. TBAF
   PIFA, then TFA
   → 2

10. Cu(TMP)₂CNLi₂
    tBuOOH
    then Ac₂O, TEA, DMAP
    → 18

11. OTIPS
    → 15

12. OTIPS
    → 17

13. CO₂Me

14. CO₂Me

15. ArN=O then Zn, AcOH
   → 11a’

16. TIPSOTf
   2,6-lutidine
   → 17