(±)-Lundurine A is an indole alkaloid that exhibits cytotoxicity in drug-resistant human oral epidermoid carcinoma cells.

Nash et al. applied the vinylogous Pictet-Spengler reaction developed in this paper to the synthesis of (±)-Lundurine A.

This method allows the installation of the eight-membered ring and quaternary carbon center in one step, which was previously unknown.

**Retrosynthesis**

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Forward Synthesis

Fisher-Indole Synthesis
Forward Synthesis

**Mechanisms:**

S1: NHNH₂·HCl

S2: OMe

S3: OH

S4: TBDPSCI Imidazole

S5: CH₂Cl₂, 0 °C

S6: NaH, Bn–Br DMF, 0 °C

S7: TBDPS

S8: Bn–Br

S9: S8

S10: Bn–Br neopentanol THF –78 °C to 0 °C
**Forward Synthesis**

1. **Grignard Addition**
   - Reaction of compound 13 with BnO-MgBr in THF, 0 °C to 23 °C, yielding 14 (78% yield).

2. **Work-up**
   - Compound 14 reacted with Me₃SiCl (1.25 equiv.) in CH₂Cl₂, 0 °C to 23 °C, yielding 15 (70% yield).

3. **Vinylogous Pictet-Spengler Cyclization**
   - Compound 15 subjected to TMSCl, resulting in 16 through path a and path b.

   **Path a**: 1,4-shift
   - Compound 7
   - Compound 8

4. **Compounds**
   - 13
   - 14
   - 15
   - 16

**Notes**
- Nomenclature and structural details are omitted for brevity.
-反应条件和产率已标注。
- Vinylogous Pictet-Spengler Cyclization involves a 1,4-shift.
- Compounds are labeled with appropriate functional groups and structural modifications.
Forward Synthesis

1. Pd/C, NH₄COOH, MeOH, 65 °C
2. Pd/C, H₂, 23 °C, MeOH/HCl
3. TBSCI, Imidazole, CH₂Cl₂/CHCl₃, 0 °C to 23 °C
(47 % yield, 3 steps)

1. MeCN, DBU, 23 °C
2. TBAF, THF, 0 °C
(54% yield, 2 steps)

1. One more Bn-deprotection
2. TBS-protection

TBS-deprotection
Forward Synthesis

1. (COCl)$_2$, DMSO
   $(i$-Pr)$_2$NEt
   $-78^\circ$C to 0°C

2. Et$_3$SiCl, DBU
   CH$_2$Cl$_2$, 40°C
   (60% yield, 2 steps)

PCWP, H$_2$O$_2$
   CH$_2$Cl$_2$, 23°C
   (63% yield, 2 steps)

Swern Oxidation

2-step tungsten-catalyzed dehomologation reaction

PCWP = Peroxotungtophosphate
Forward Synthesis

1. TsNHNH₂, p-TsOH
   CH₂Cl₂, 23 °C

2. BF₃·Et₂O
   CH₂Cl₂, 80 °C
   (61% yield, 2 steps)

1. LDA, THF
   PhSO₂Me, –78 °C

2. K₂CO₃, PhMe
   100 °C
   (17% yield, 2 steps)

(±)-lundurine A (1)