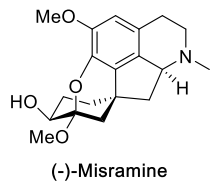


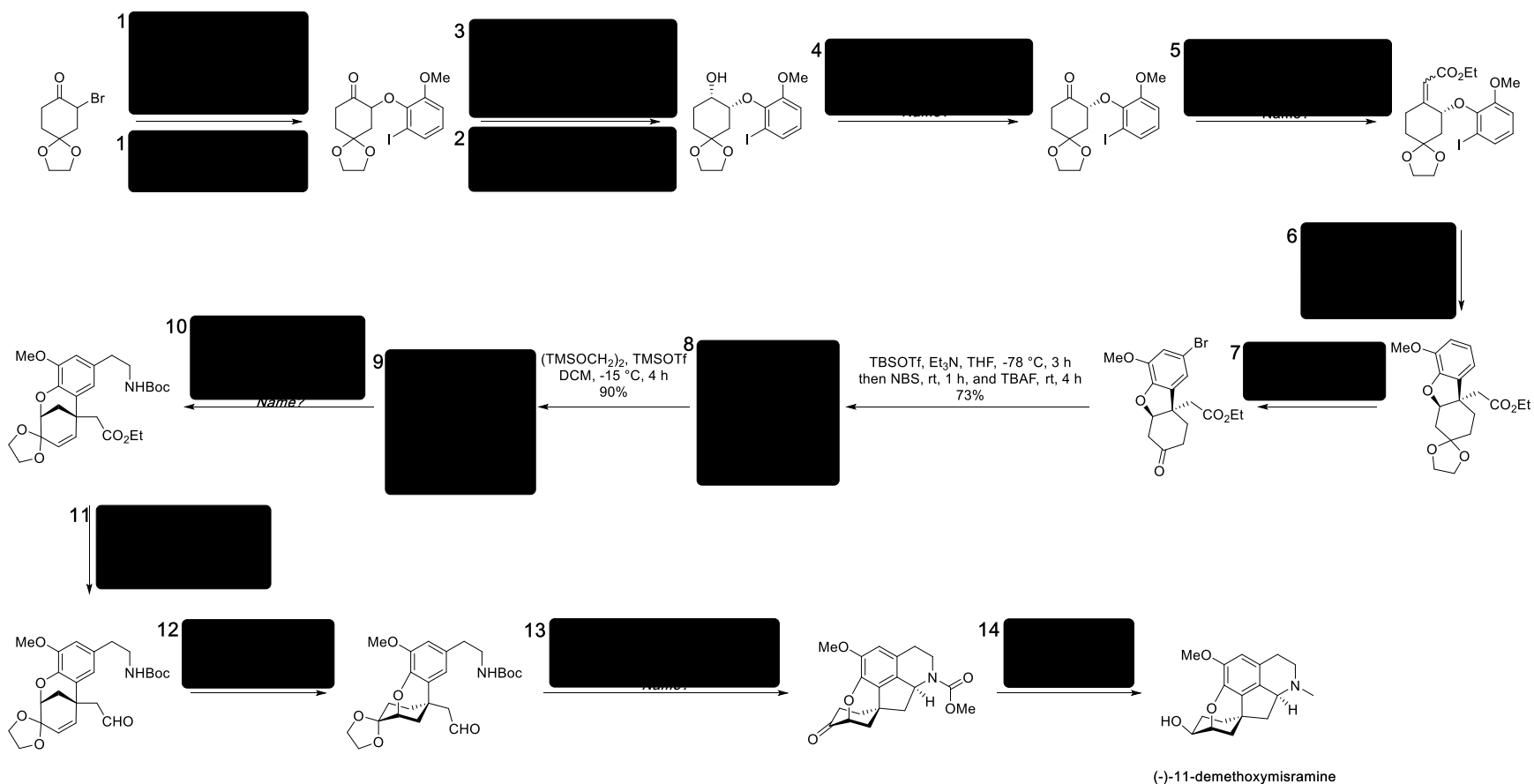
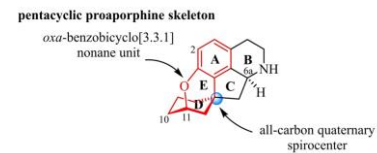
Total Synthesis of (-)-Misramine

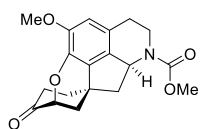
Adv. Synth. Catal. 2020, 362, 1 – 7



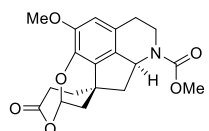
Proaporphine alkaloids

- tetracyclic ring system containing a spiro-cyclohexadienone ring
- found in Egyptian *Roemeria hybrida* and *R. dodecandra* (Papaveraceae) by Shamma and co-workers in 1985
- enantioselective total synthesis by Yoshida and Takao et al. in 2018 : only total synthesis of pentacyclic proaporphine alkaloids
 - => organocatalyzed asymmetric intramolecular Friedel-Crafts-type 1,4-addition as the key step (73% ee)
 - => 24 steps with 2.0% overall yield
- asymmetric construction of the chiral all-carbon quaternary spirocenter remains a challenge

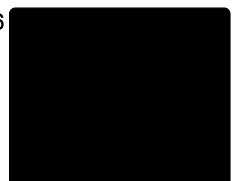




15

DIBALH, DCM
-78 °C, 1.5 h

16

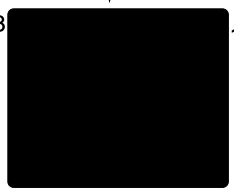


+

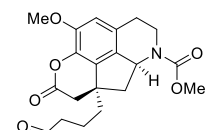


1. HCl, THF, rt, 4 h
2. NaClO₂, Na₃PO₄
2-methylbut-2-ene/tBuOH/THF/H₂O (3:3:3:1)
rt, 5 h, *Name?*
3. EDCI, DMAP, DCM, rt, 5 h, 65%

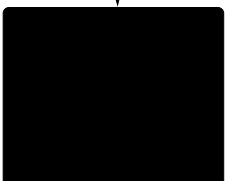
18



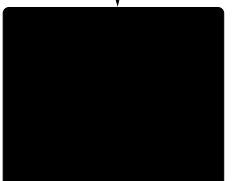
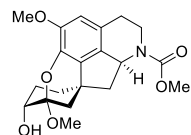
19

SmI₂, tBuOH
THF (0.006M), rt, 1.5 h
Name?

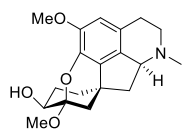
21



+

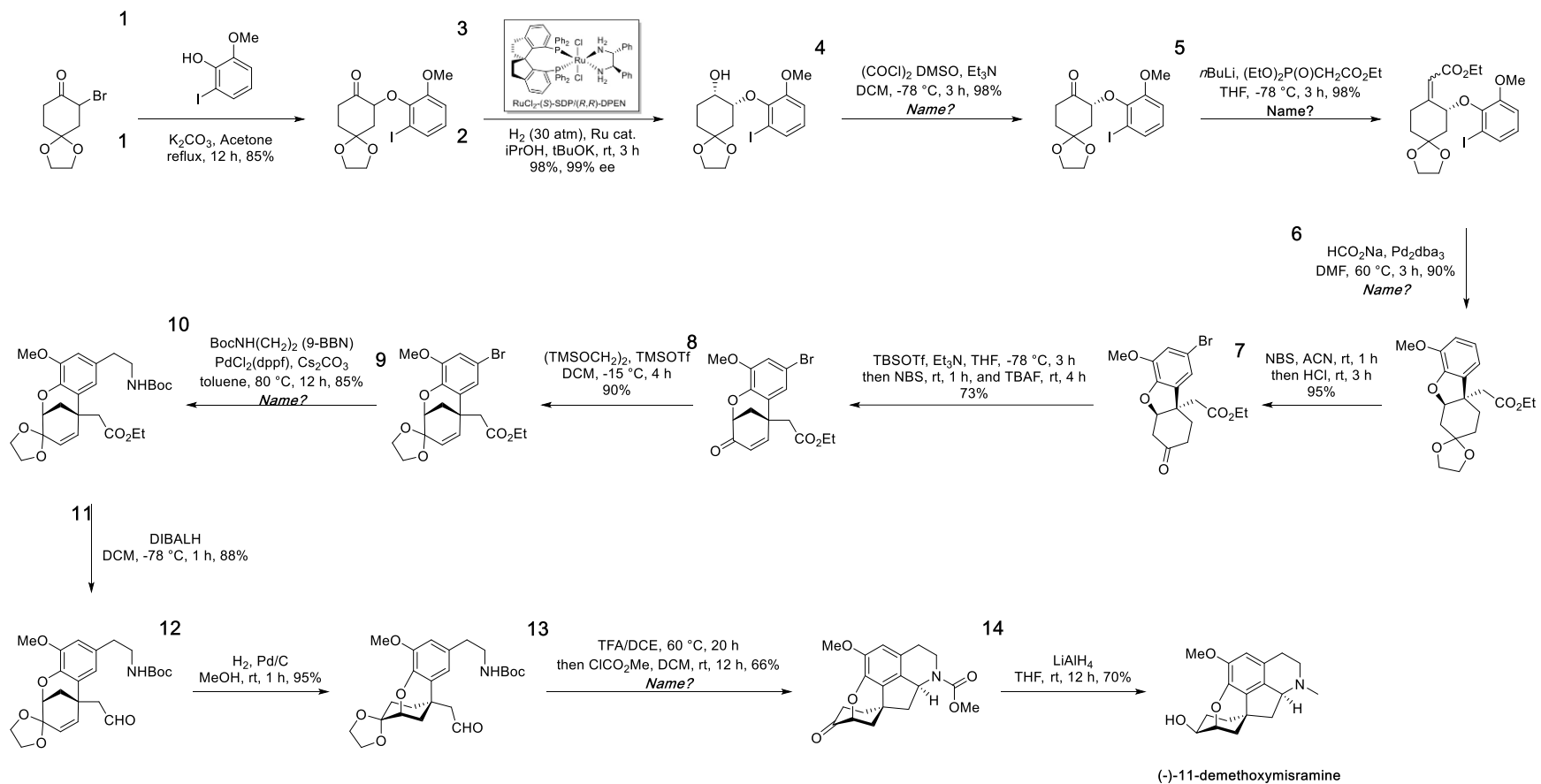
CH(OMe)₃, CSA
MeOH, rt, 4 h, 85%

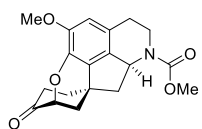
22



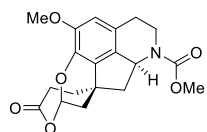
(-)-Misramine

SOLUTIONS

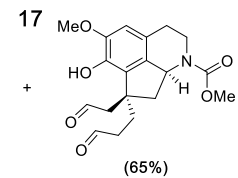
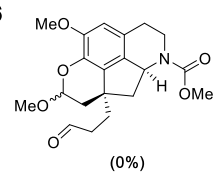




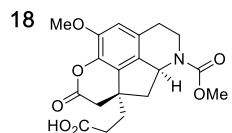
15
 $m\text{CPBA}$, LiCO_3
 DCM, rt, 1 h, 80%
Name?



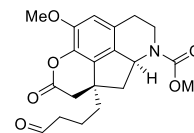
16
 DIBALH , DCM
 -78°C , 1.5 h



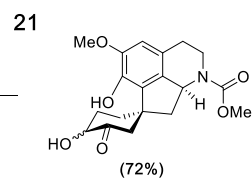
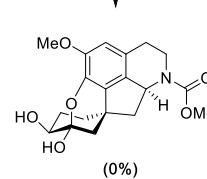
1. HCl , THF, rt, 4 h
 2. NaClO_2 , Na_3PO_4
 2-methylbut-2-ene/ tBuOH / THF / H_2O (3:3:3:1)
 rt, 5 h, *Name?*
 3. EDCI , DMAP , DCM, rt, 5 h, 65%



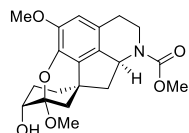
19
 1. BH_3 ·THF, 0°C , 3 h, 85%
 2. PCC , DCM, rt, 5 h, 78%



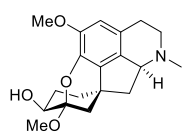
SmI_2 , tBuOH
 THF (0.006M), rt, 1.5 h
Name?



$\text{CH}(\text{OMe})_3$, CSA
 MeOH, rt, 4 h, 85%



22
 1. $(\text{COCl})_2$, DMSO, Et_3N
 DCM, -78°C , 2 h, 92% *Name?*
 2. LiAlH_4 , THF, rt, 12 h, 89%



(-)-Misramine