Gram-Scale Enantioselective Formal Synthesis of Morphine

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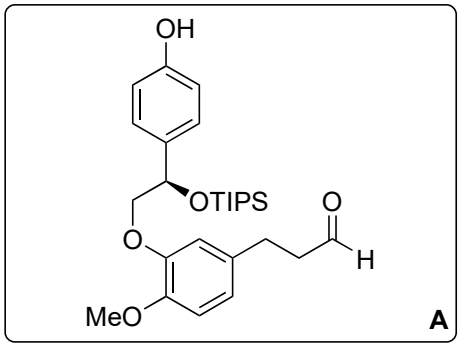
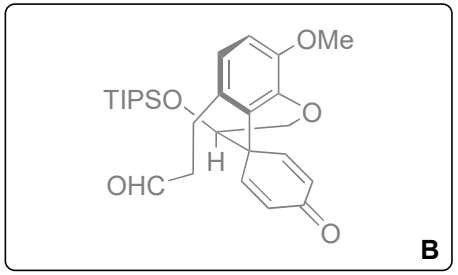
Angew. Chem. Int. Ed. **2014,** *53*, 13498 –13501



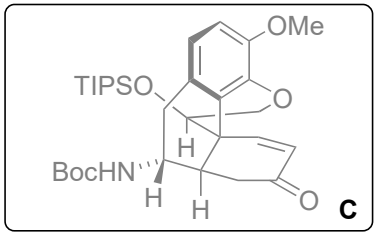
1

1) $PhI(OAc)_2$, TFE, –40 °C

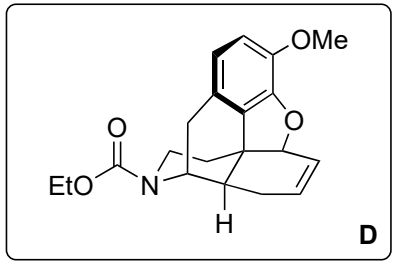


2–4

2) DBU (0.1 equiv), CH_2Cl_2
3) $NaClO_2$, NaH_2PO_4, *t*-BuOH/H_2O, 2-methyl-2-butene
4) DPPA, NEt_3, *t*-BuOH

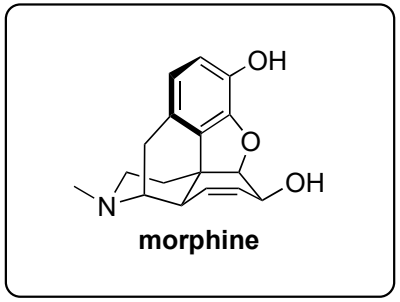


5–10



D

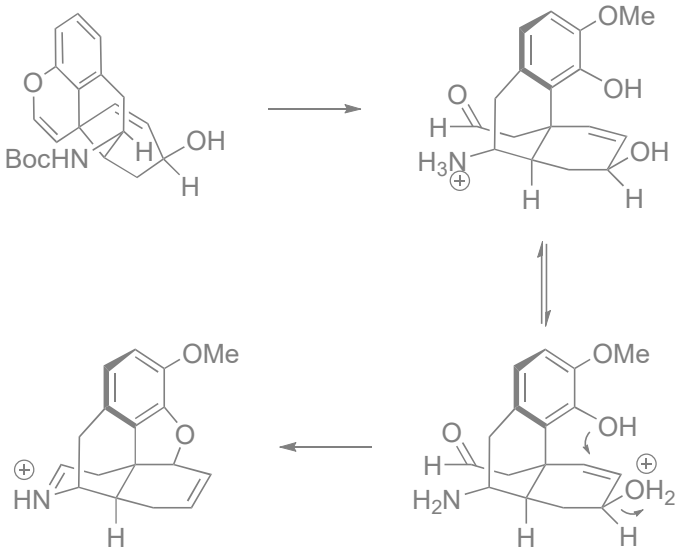
seven steps



morphine

5) TBAF, THF
6) MsCl, Et_3N, DMAP, CH_2Cl_2
7) DBU, MeCN, 85 °C
8) $NaBH_4$, $CeCl_3$, MeOH
9) HCl (aq.), 80 °C, MW
10) $NaBH(OAc)3$, AcOH/DCE *then* $ClCO_2Et$, Et_3N

Please provide a mechanism for step 9.



Bonus question
Please develop a route to convert **D** into morphine.

Taber, D. F.; Neubert, T. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **2002**, *124*, 12416-12417.

11) $[(C_8H_{17})_3NCH_3]^+{}_3[PO_4[W(O)(O_2)_2]_4{}^{-3}$, H_2O_2
12) PhSeSePh, $NaBH_4$
13) $NaIO_4$, H_2O
14) Na_2CO_3
15) MnO_2
16) $LiAlH_4$
17) BBr_3