Morphine and Codeine

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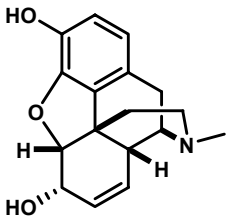
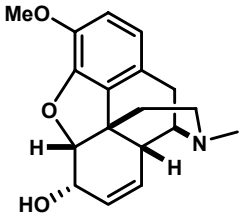
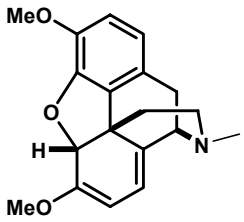


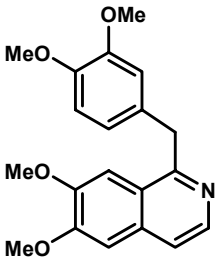
Morphine



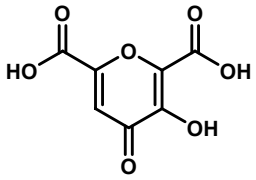
Codeine



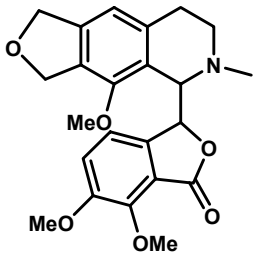
Thebaine



Papaverine



Meconic Acid



Noscapine

Raw opium contains approximately 25 different alkaloids by weight, depending on the variety. The chief alkaloids are Morphine (4-21%), Codeine (0.8-2.5%), Thebaine (0.5-2%), Papaverine (0.5-2.5%), Noscapine (4-8%), Meconic Acid (3-5%).

For excellent reviews on Morphine and Codeine, see

1. Hudlicky, T. *et al Studies in Natural Products Chemistry*, 1996, *18*, 43

2. Taber, D.F. *et al Strategies and Tactics in Organic synthesis,* 2004, *5*, 353

3. Maier, M. *Organic Synthesis Highlights II*, 1995, 357

4.Novak, B.H. *et al Curr. Org. Chem.* 2000, 4, 343

5. Blakemore, P.R. *et al*, *Chem. Comm.* 2002, 1159

6. Zezula, J. *et al*, *Synlett,* 2005, 388

The following work will be included in this talk due to the time limitation.

Gates	1952	(-)-Morphine
Rice	1980	(-)-Dihydrocodeinone
Evans	1982	O-Me-thebainone-A
Fuchs	1988	Codeine
Tius	1992	Thebainone-A
Parker	1992	Dihydrocodeinone
Overman	1993	(-)-Dihydrocodeinone
Mulzer	1996	(-)-Dihydrocodeinone
Parsons	1996	Morphine
White	1997	(+)-Morphine
Hudlicky	1998	10-hydroxy-*ent*-epi-dihydrocodeinone
Cheng	2000	Desoxycodeine-D
Ogasawara	2001	(-)-Dihydrocodeinone ethylene ketal
Taber	2002	(-)-Morphine
Trost	2002	(-)-Codeine
Michels	2005	14-Hydroxycodeinone

Morphine and Codeine

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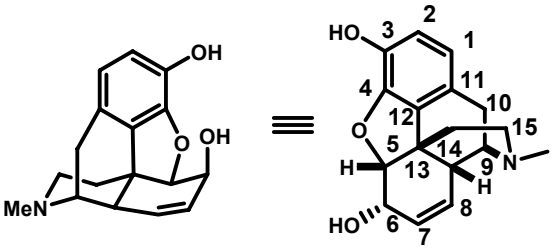
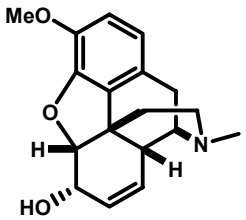
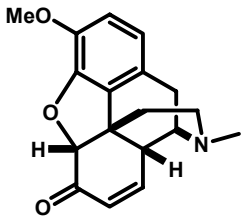


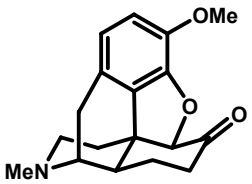
(-)-Morphine



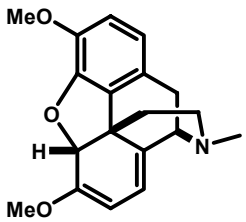
(-)-Codeine



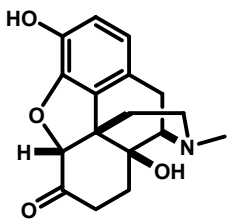
Codeinone



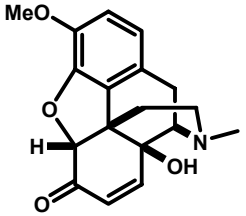
Dihydrocodeinone



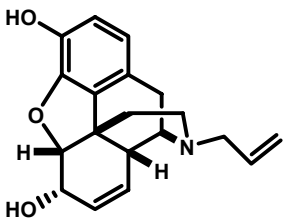
Thebaine



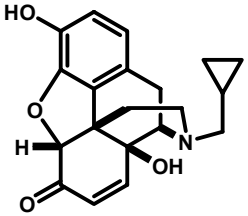
Noroxymorphone



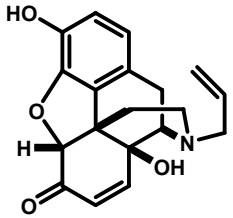
Hydoxycodeinone



Nalorphine



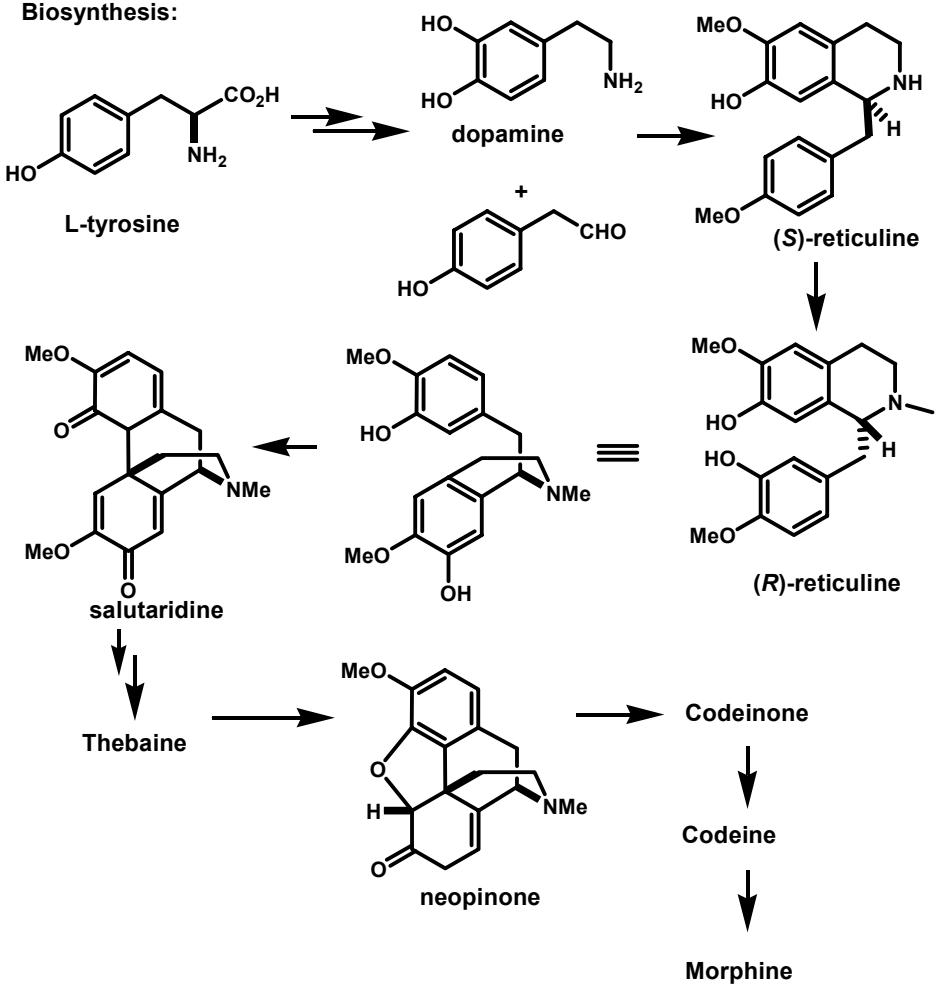
Naltrexone



Naloxone

Morphine and codeine are the principal ingredients from opium poppy latex extract. The legal medicinal use of morphine in the US is more than 80 tons/year and the world wide illicit market for narcotics is probably more than $760 billion.

Biosynthesis:



Morphine and Codeine

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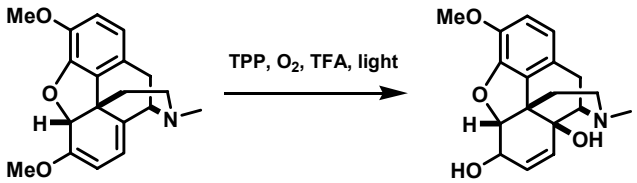
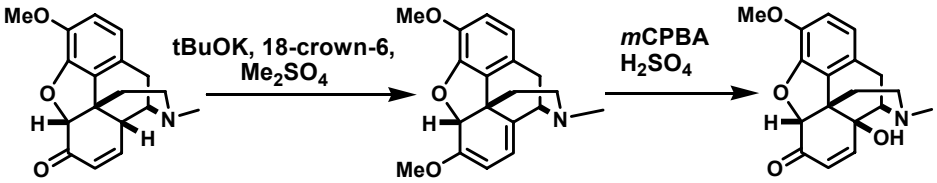


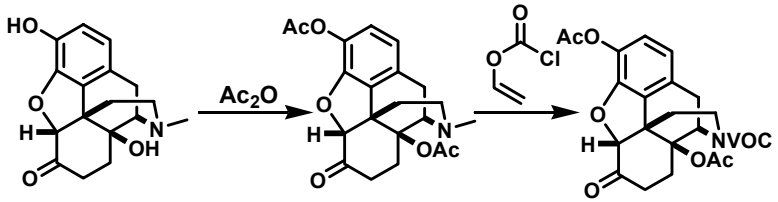
Thebaine

Tetrahedron Lett. 1994, *31*, 5727

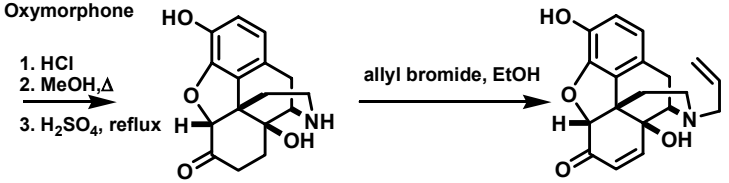


Heterocycles, 1998, *49*, 43

J. Org. Chem., 1996, *61*, 6774

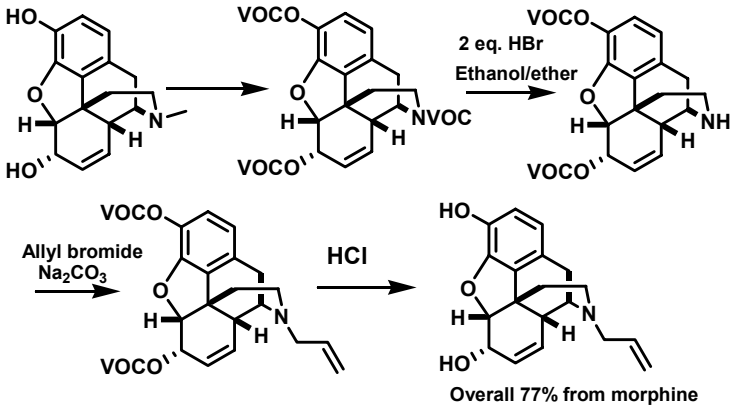


Oxymorphone

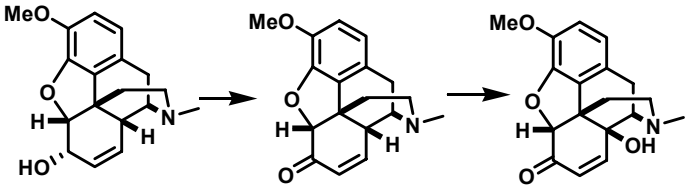


Tetrahedron Lett. , 1977, 1567

Naloxone



Tetrahedron Lett.. 1977, 1571



(-) Codeine

J. Am. Chem. Soc. 2005, *ASAP*

Morphine and Codeine

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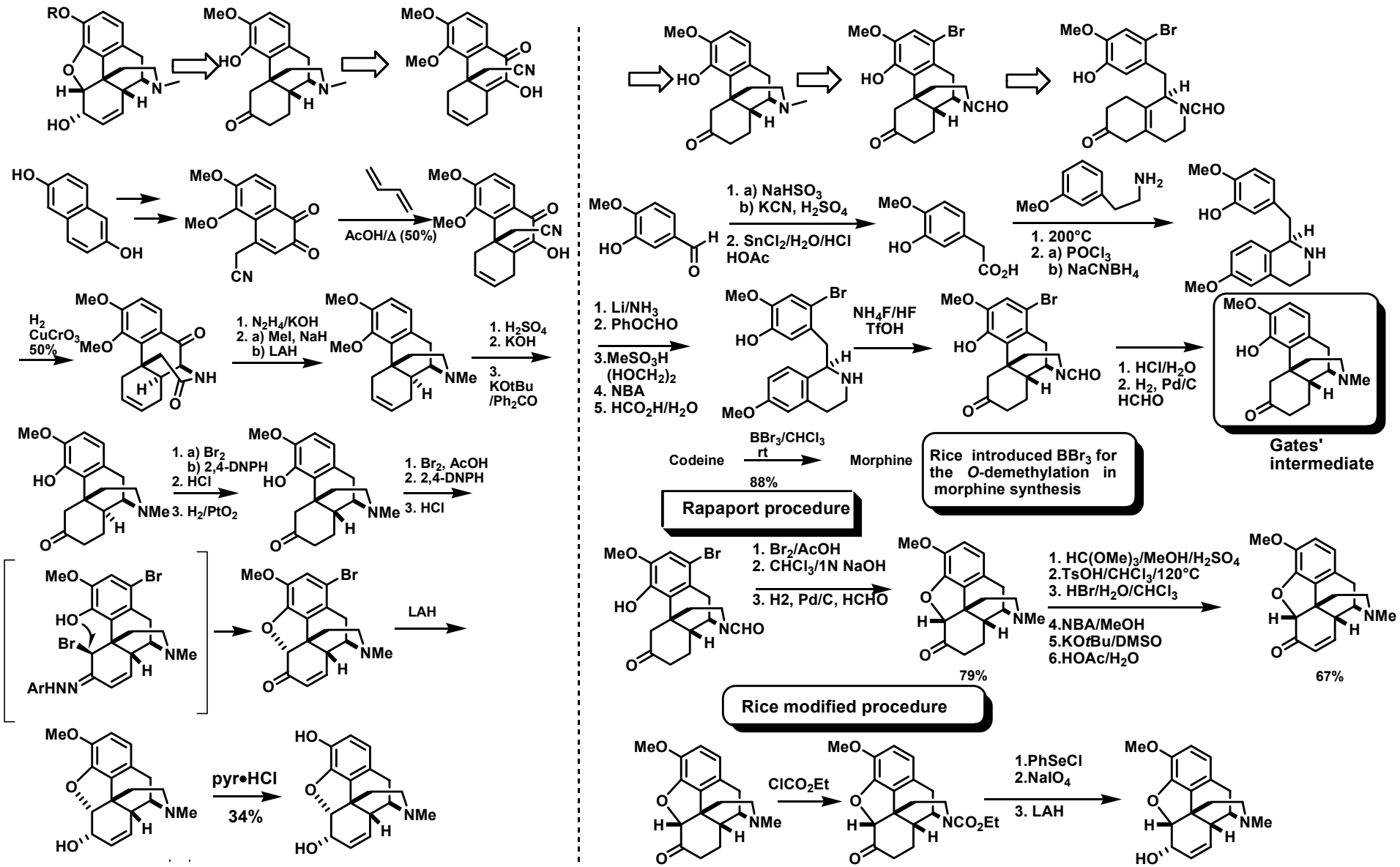

Gates, *JACS*, 1952, *74*, 1109

Rice, K.C. *Heterocycles* 1977, *6*, 1157
JOC, 1980, *45*, 592

Rapaport, H. *J. Med. Chem.* 1976, *19*,1171

Morphine and Codeine

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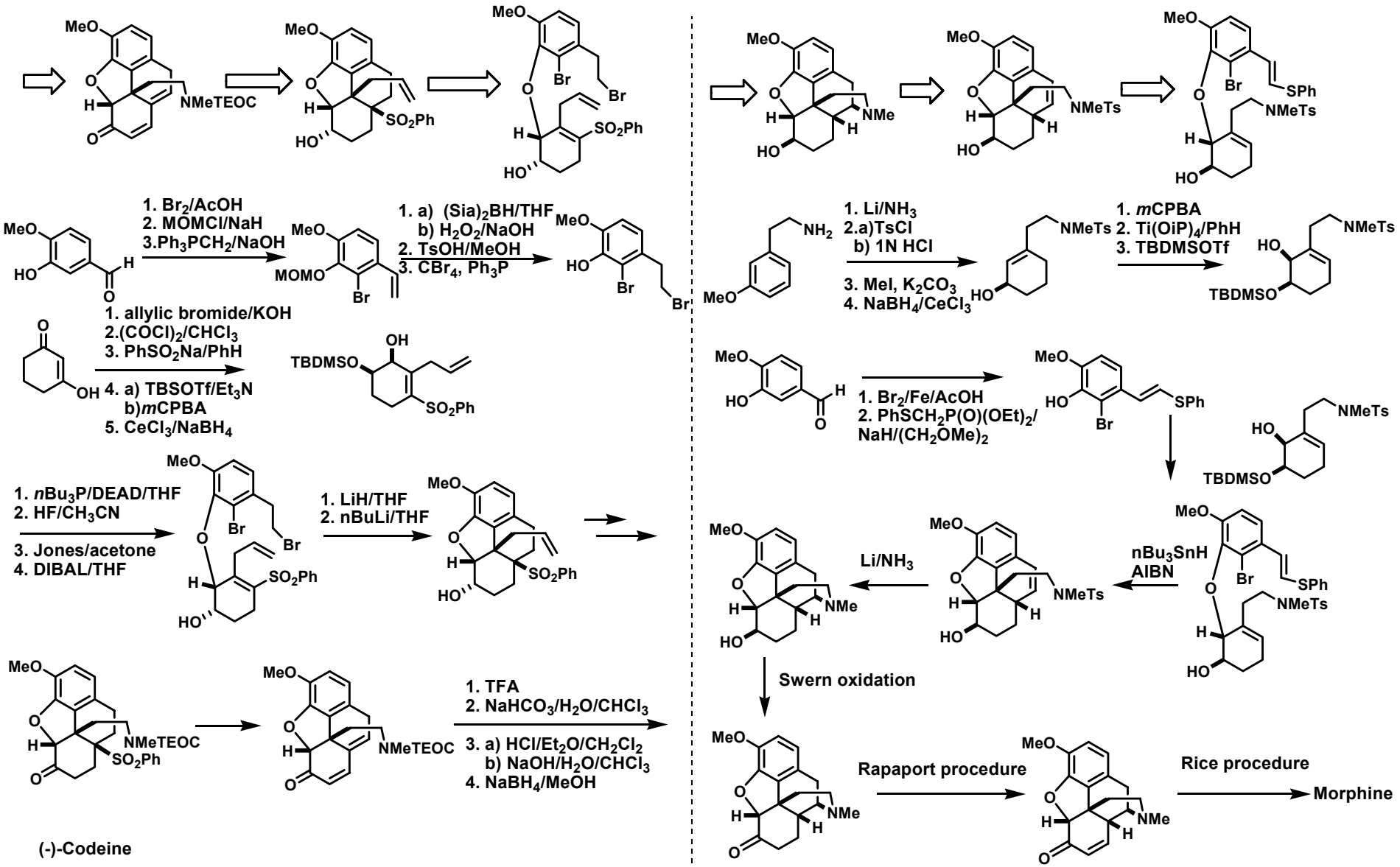

Fuchs, P.L. *JOC*, 1987, *52*, 473

Parker, K.A. *JACS,* 1992, *114,* 9688

Morphine and Codeine

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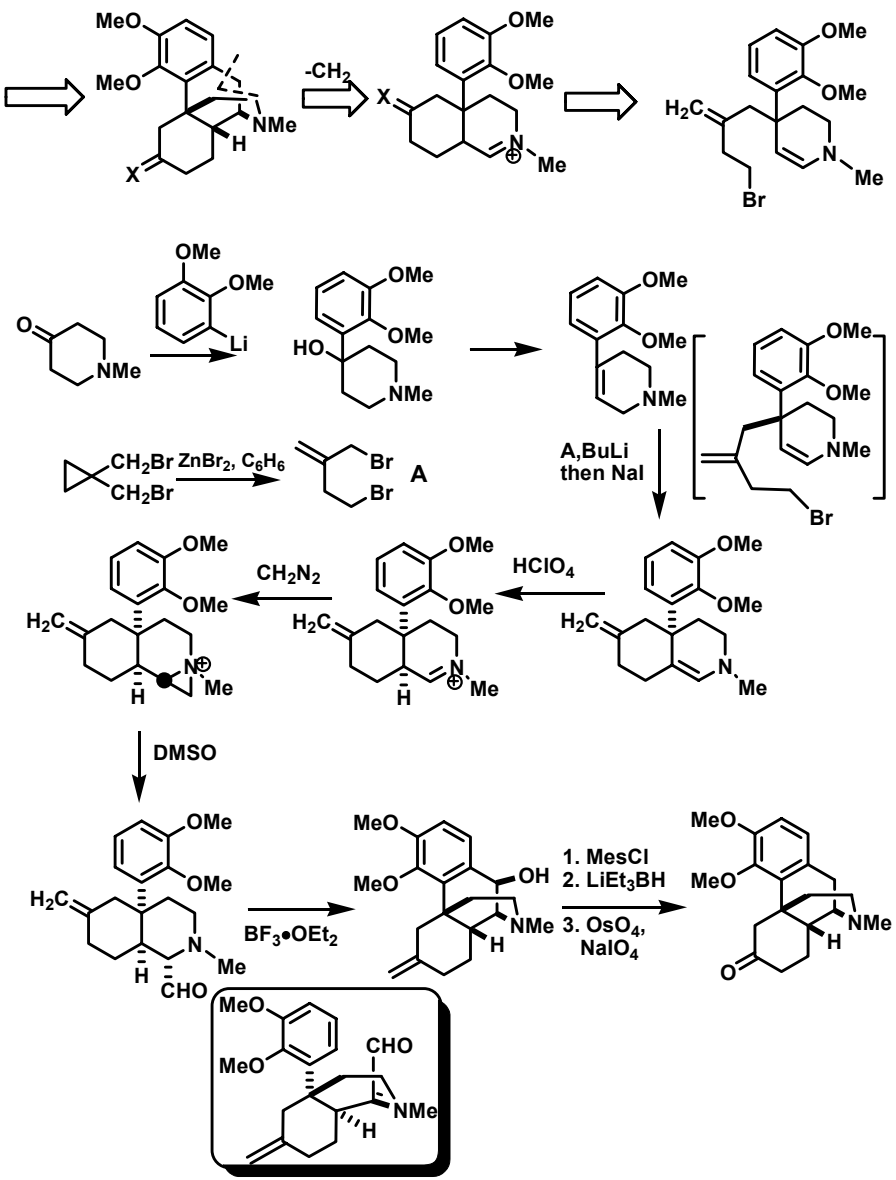

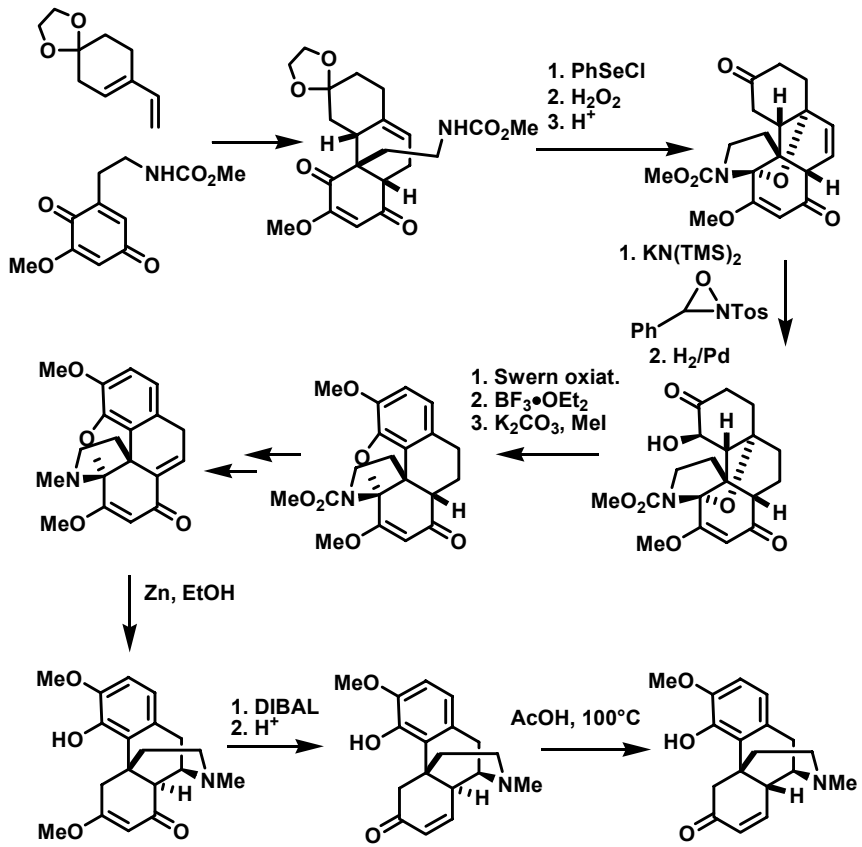

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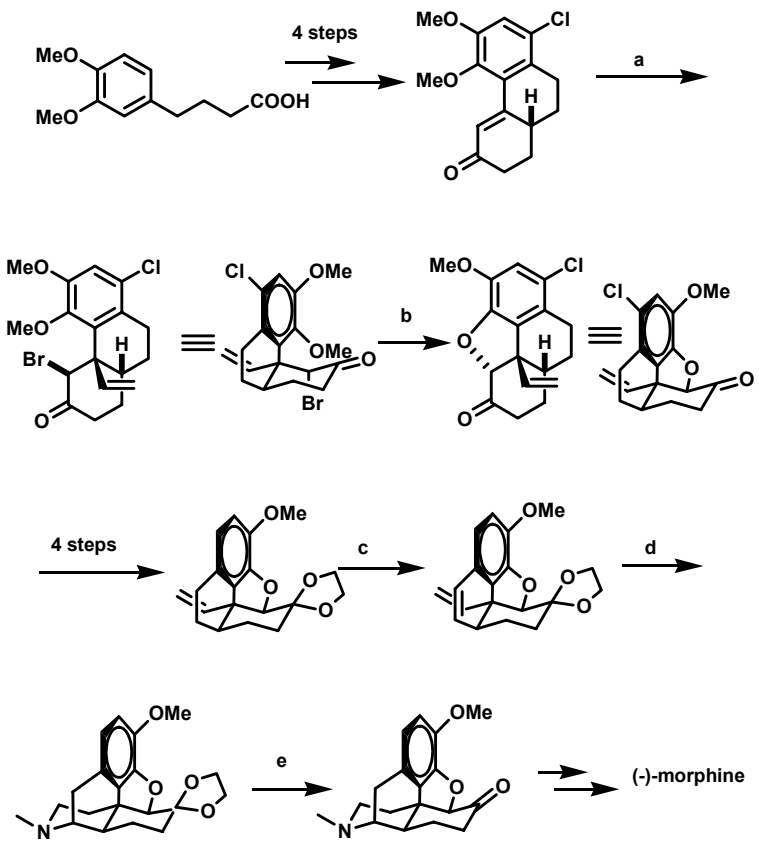
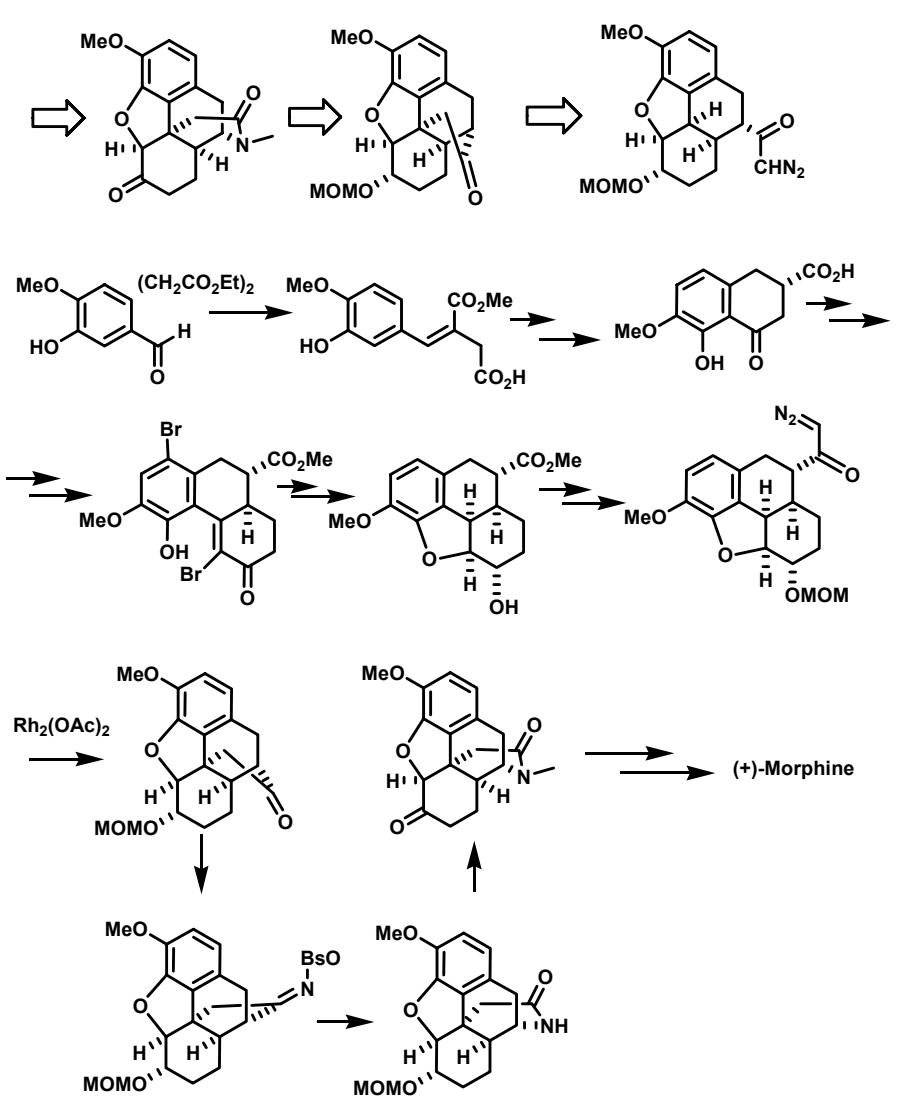


a) $(H_2C{=}CH)_2CuMgCl$, THF, - 78 °C to 0 °C; ii) TMSCl, Et_3N, 0 °C to 25 °C; iii) NBS, THF (63-80%). b) DMF, 140 °C (99%). c) NBS, $(PhCOO)_2$, CCl_4, rflx (68 - 81%). d) Li, NH_3, THF, *t*-BuOH (79 %). e) 3 N HCl, 90 °C (95 %).



Mulzer, J. *ACIE*, 1996, *35*, 2835
Synthesis, 1998, 653

White, J. *JOC*, 1997, *62*, 5250

Morphine and Codeine

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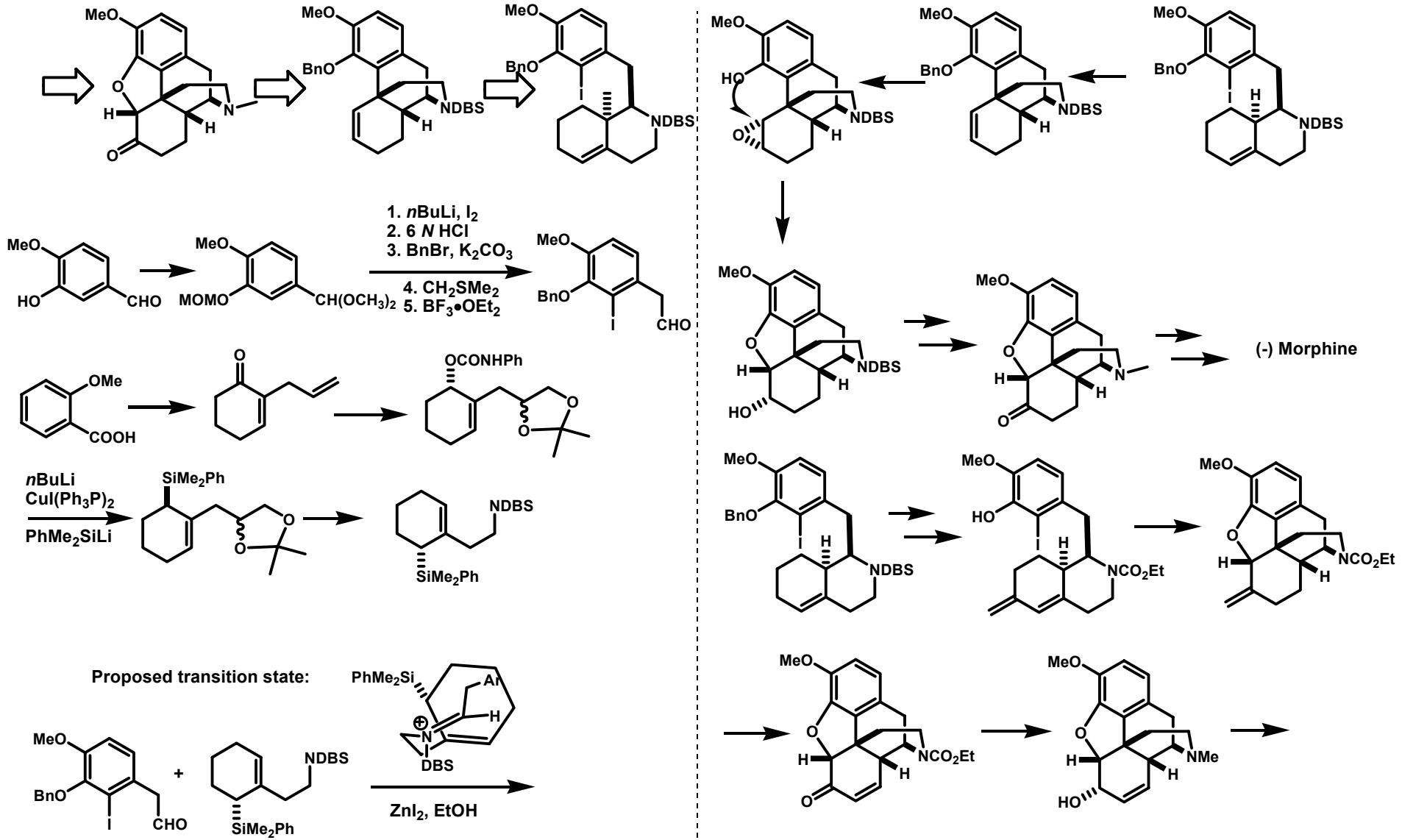

Morphine and Codeine

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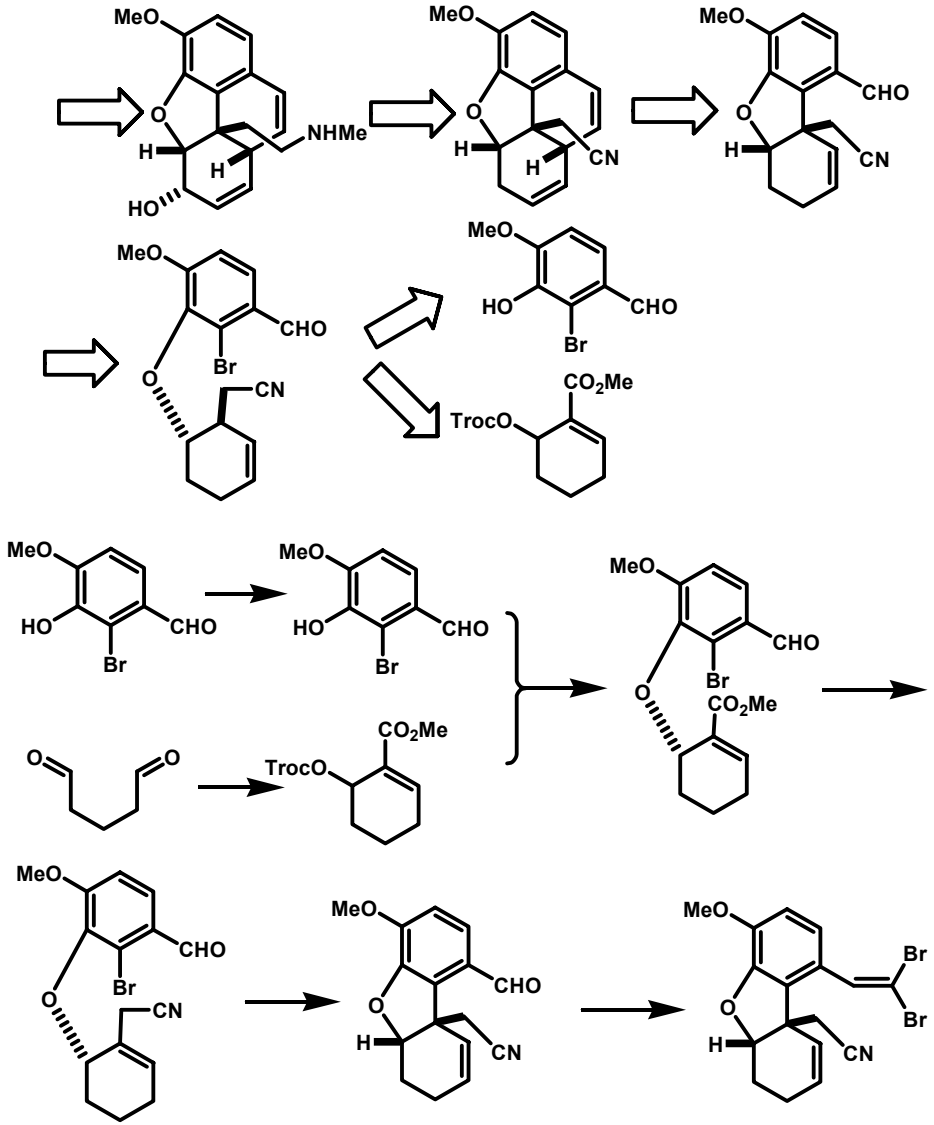

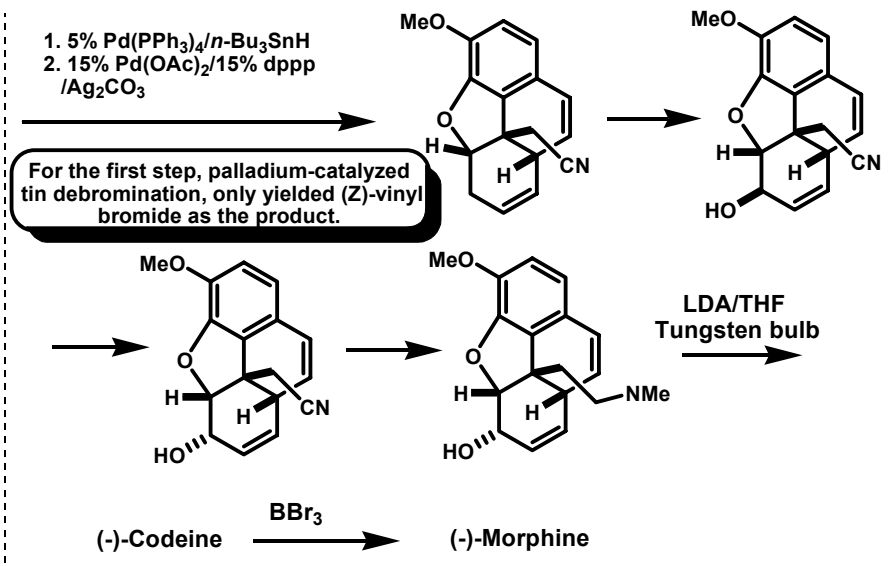

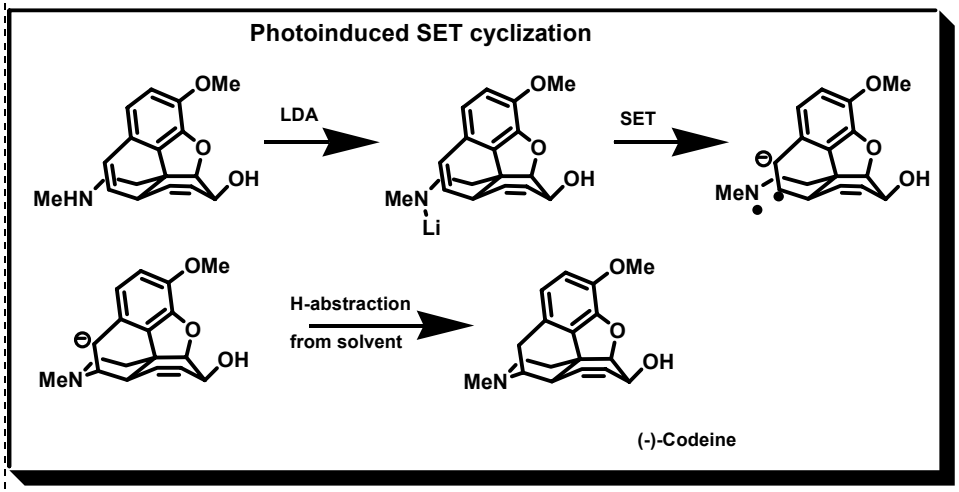

Trost, B.M. JACS, 2002, 124, 14542

Morphine and Codeine

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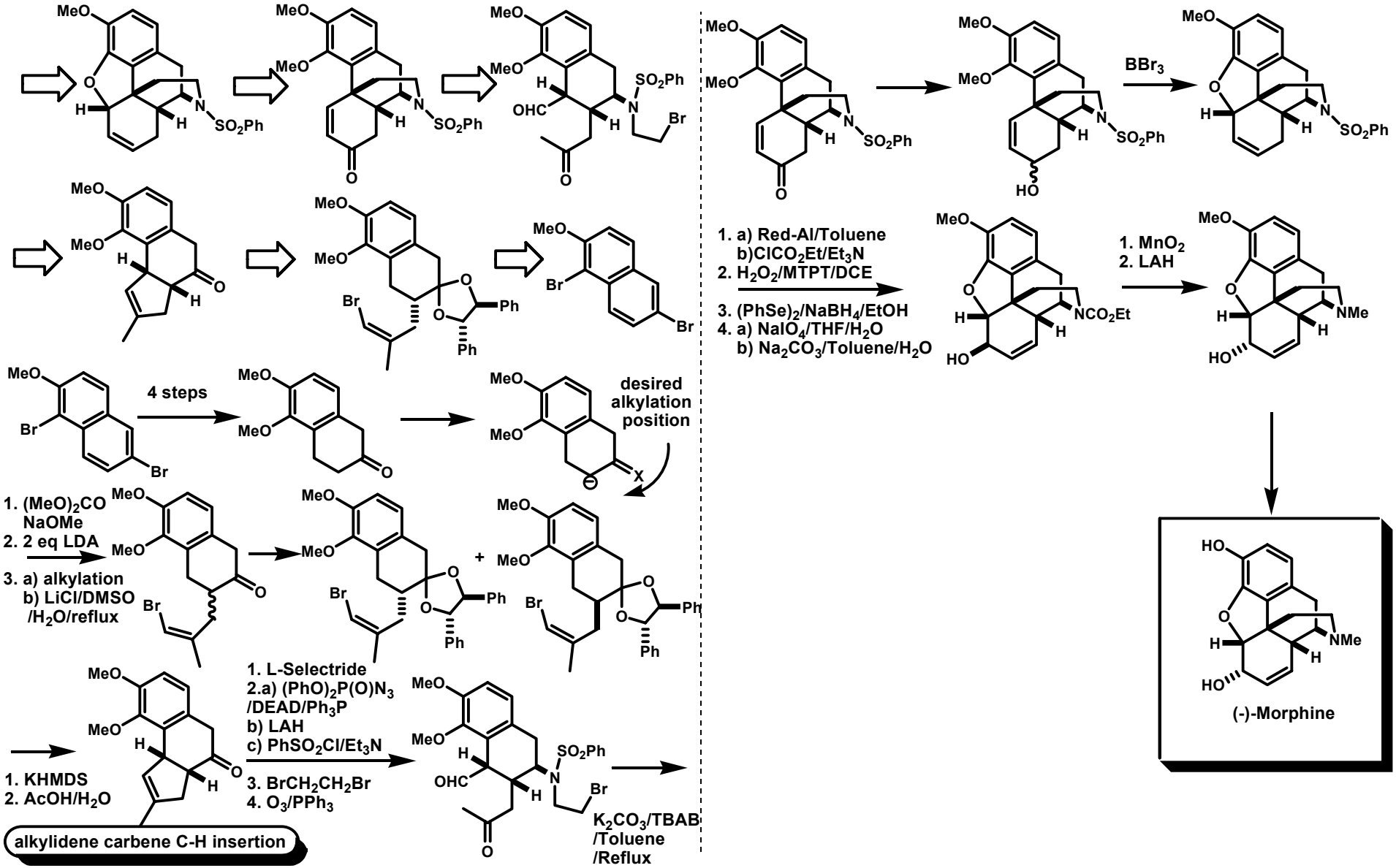

Taber, D.F. *JACS*, 2002, *124*, 12416

Morphine and Codeine

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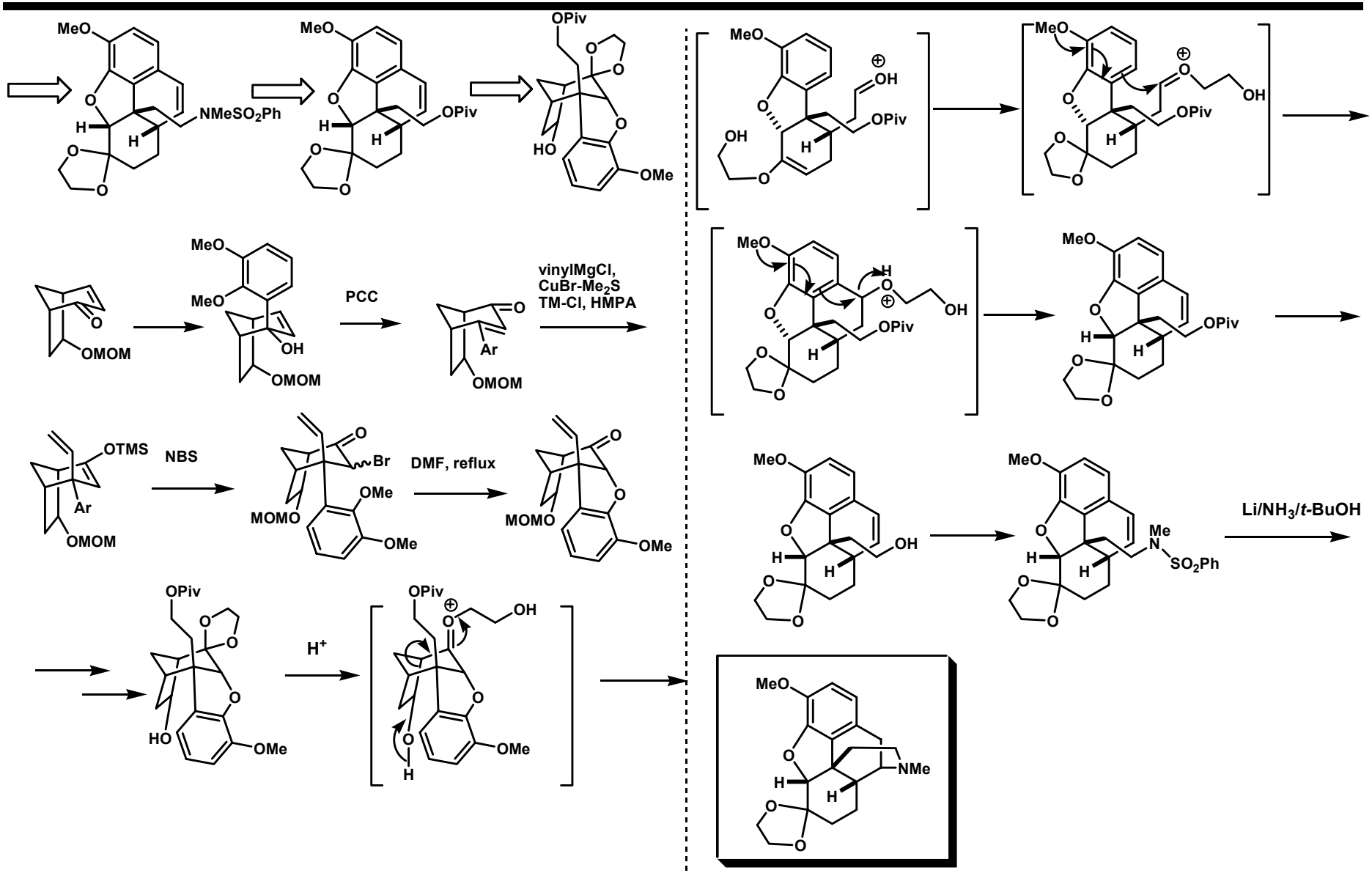

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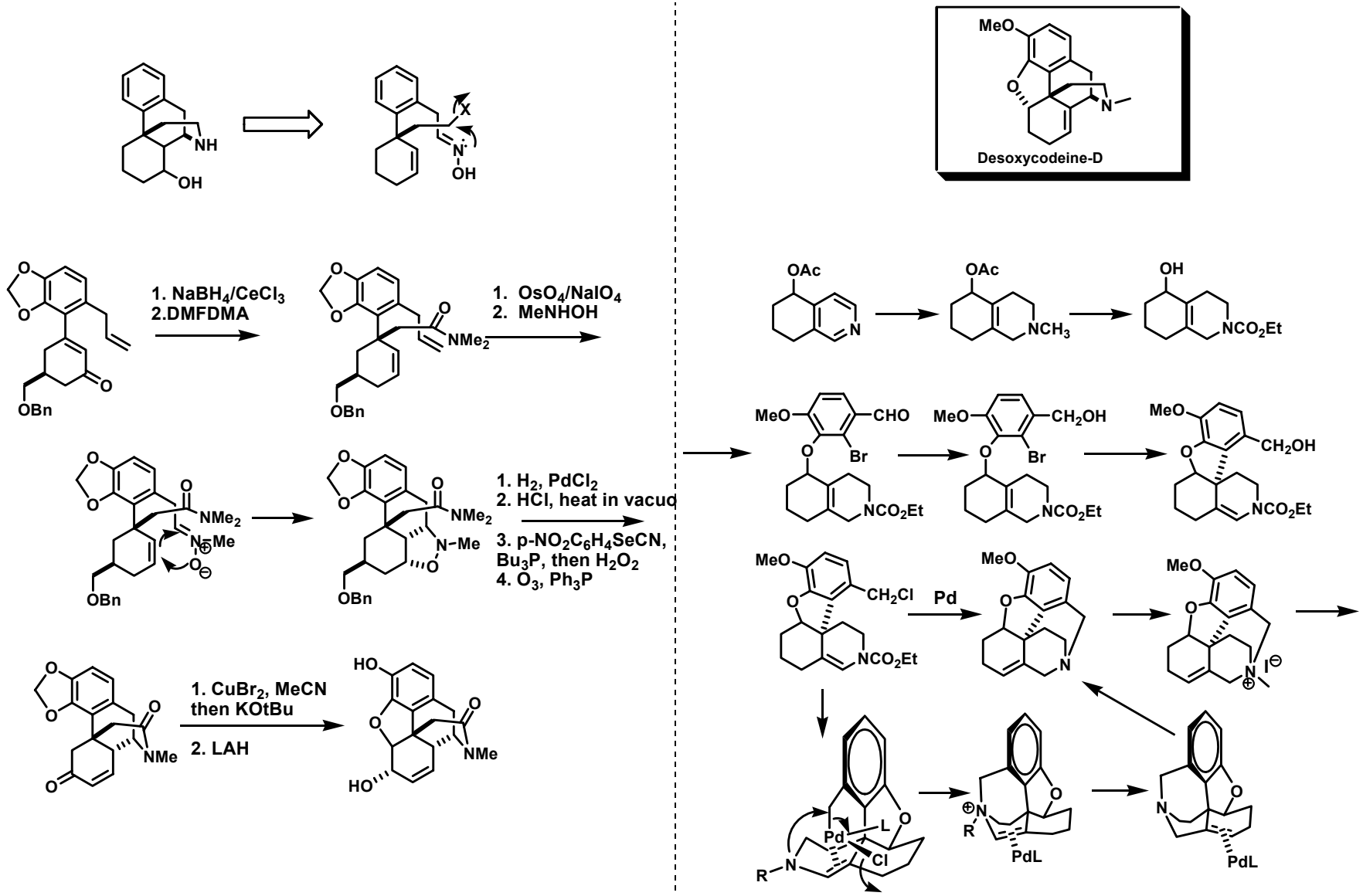

Morphine and Codeine

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