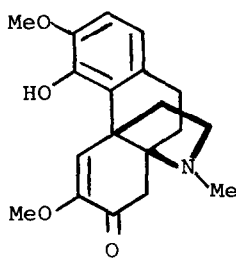
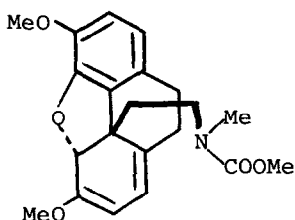


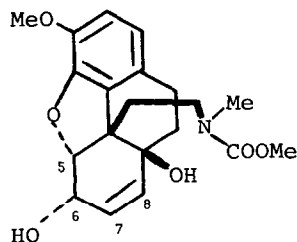
yield by photocyclization of a bromosecoreticoline derivative, and it has been converted by transesterification into (\pm)-cepharamine (3).⁸



9



10



11

Dienone 4b was reduced with NaBH_4 (CH_3OH , 25° , 1 hr) and the crude dienol was cyclized by sequential treatment⁹ with cold SOCl_2 /pyridine followed by hot aqueous NaOH , to afford (\pm)-N-methoxycarbonyl-9,17-secothebaine (10) in 57% over-all yield [mp 119 - 120° ; nmr (CDCl_3) δ 6.59 (d, $J=8.5$), 6.55 (d, $J=8.5$), 5.51 (d, $J=6$, H-8), 5.50 (s, H-5), 5.00 (d, $J=6$, H-7); m/e 371 (M^+), 282, 255, 116, 102 (base peak)].^{6a} All attempts to hydrolyze 10 to the corresponding secocodeinone derivative using methods developed¹⁰ for thebaine itself were unsuccessful. However, reaction of 10 with photochemically generated singlet oxygen (Rose Bengal, $\text{CHCl}_3/\text{CH}_3\text{OH}$, 12°) and immediate reduction of the crude product with NaBH_4 (CH_3OH , 25° , 15 min) gave (\pm)-N-methoxycarbonyl-14-hydroxy-9,17-secocodeine (11) in 40% yield [mp 149 - 150° ; nmr (CDCl_3) δ 6.63 (d, $J=8.5$), 6.54 (d, $J=8.5$), 5.82 (br d, $J=10$, H-7), 5.54 (dd, $J=10$ and 3.5 , H-8), 5.08 (m, H-5), 4.58 (m, H-6); m/e 375 (M^+), 277, 276 (base peak), 244, 241].^{6b}

The stereochemistry assigned to 11 was confirmed by nmr decoupling experiments at 270 MHz. Successive irradiation of the signals assigned to H-7, H-8, and H-5 indicated that H-6 was axial and was coupled to four protons: vicinally coupled to the equatorial H-5 ($J_{5,6}=5.5$ Hz), vicinally coupled to the vinylic H-7 ($J_{6,7}=2$ Hz), long-range coupled to the vinylic H-8 ($J_{6,8}=3.5$ Hz), and vicinally coupled to the adjacent OH ($J=10$ Hz). These values and assignments were in good agreement with those reported¹¹ for codeine and 14-hydroxycodeine.

The unique directing effect of Tl(III) for para-ortho oxidative coupling observed² in the reticoline system is thus extended to the seco derivatives, but somewhat surprisingly with little difference in either absolute or relative yields of the isomeric coupling products. The implications of these results in terms of the mode of action of TFA in phenol coupling, as well as the extension of the method to the synthesis of other potentially useful morphine alkaloid analogs, are currently under study.

Acknowledgement. This work was supported by Public Health Service Grant DA 01962 from the National Institute on Drug Abuse.

References and Notes

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(Received in USA 13 April 1979)