IMPROVED SYNTHESIS OF (+)-MORPHINE, (+)-CODEINE AND (+)-HEROIN

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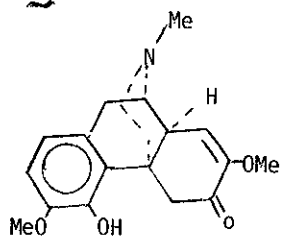
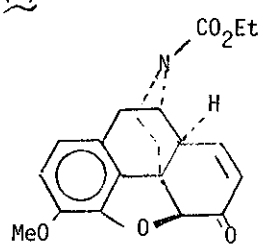
Natural (-)-sinomenine (1), a major alkaloid of Sinomenium species, has been converted by K. Goto, et al.[1] in an admirable effort into (+)-morphine (3) and (+)-codeine (4). A much improved procedure for preparing these enantiomers of these important opium alkaloids, including the preparation of (+)-heroin (5), will now be presented. Sinomenine (1) is first converted into the carbamate of (+)-norcodeinone (2) which can easily be reduced to (+)-codeine (4) with lithium aluminum hydride. Conversion into (+)-morphine (3) can be accomplished by O-demethylation of 4 with boron tribromide[2]. O-diacetylation of 3 affords (+)-heroin (5).



1



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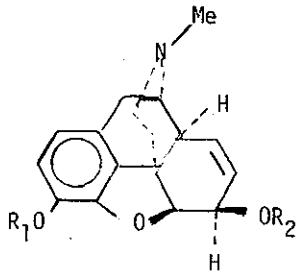

3 $R_1=R_2=H$; 4 $R_1=Me, R_2=H$
5 $R_1=R_2=Ac$

Details on this novel reaction sequence and biological data obtained with compounds 3, 4 and 5 will be discussed.

1. K. Goto and I. Yamamoto, Proc. Japan Acad. 36, 145 (1960); K. Goto, Monograph on "Sinomenine" by the Tokyo Kitasato Institute, 1964.

2. K. C. Rice, J. Med. Chem., 20, 164 (1977).