STEREOCHEMISTRY OF THE DIBENZOPYRROCOLINE ALKALOIDS CRYPTAUSTOLINE AND CRYPTOWOLINE

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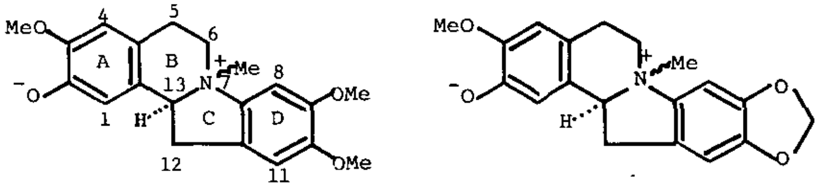
Abstract——Stereochemistry of the dibenzopyrrocoline alkaloids, (-)-cryptaustoline (1) and (-)-cryptowoline (2), isolated from the Australian shrub Cryptocaria bowiei is deduced both as 7R,13S configuration with cis B/C ring structure based on the analysis of proton-nmr spectra of synthetic materials.

In 1952 Ewing, Hughes, and co-workers reported the isolation of two unique quaternary alkaloids, (-)-cryptaustoline (1) and (-)-cryptowoline (2), from the Australian shrub Cryptocaria bowiei (Figure 1). These are only known examples of this class of alkaloids[2] and are believed to be generated in nature from a 1-benzylisoquinoline precursor by intramolecular phenolic oxidative coupling to form the bond between 7-nitrogen and aromatic 7a-carbon.[3] Stereochemistry of two alkaloids, however, has been determined only at C-13 center as S,[4] while both the relative and the absolute configuration of the quaternary 7-nitrogen center remain



(-)-cryptaustoline (1)

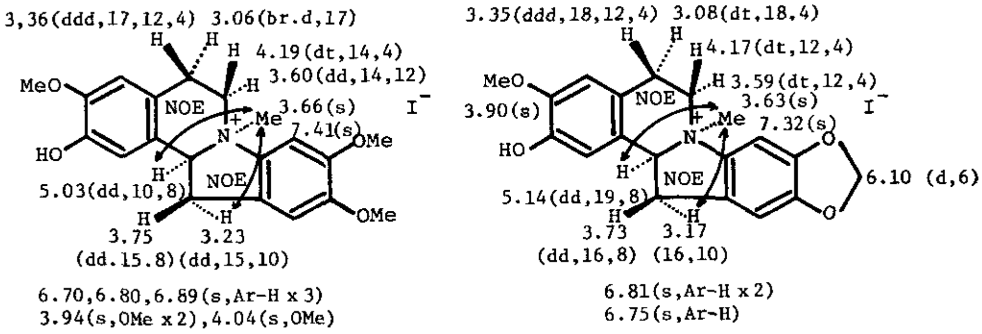
(-)-cryptowoline (2)

Figure 1

these alkaloids has been completed using the 1-benzylisoquinoline precursors in which the construction of the quaternary nitrogen center has been carried out either directly by coupling between 7-tertiary nitrogen and 7a-carbon or indirectly by coupling between 7-secondary nitrogen and 7a-carbon followed by treatment with methylating agent. In these conversions, it was found that the same relative configuration identical to that of the natural products was consistently generated in a stereoselective fashion regardless of the methods employed.[4,5] In relation to development of a new methodology for the synthesis of these alkaloids,[6] we examined the stereochemistry of these alkaloids using synthetic iodonium substrates by ^{1}H-nmr analysis which allowed us to deduce the natural configuration of both alkaloids as 7R,13S.

Complete ^{1}H-nmr spectral assignment of both alkaloids were obtained by virtual decoupling and NOE experiments[7] and the spectral assignments were obtained as shown (Figure 2). Thus, two signals at δ 5.03 and 3.23 for 1 and at δ 5.14 and 3.17 for 2 assigned to 13-αH and 12-αH, respectively, exhibited distinct NOE with the methyl group on the 7-nitrogen. Moreover, 13- H exhibited apparent NOE with 6-αH at δ 3.60 for 1 and at δ 3.59 for 2, respectively, though NOE between 6-αH and 7-methyl group could not be unambiguously observed due to their proximal chemical shifts. These clearly indicated that these four centers are disposed in spacially proximal cis relationship one another indicating cis B/C ring structures, respectively.

Since the configuration of C-13 center of the natural alkaloids has been determined as S by correlation to (S)-laudanosoline,[4] the present assignment using racemic substrates readily allows us to deduce the natural configuration of the quaternary 7-nitrogen center as R with cis B/C ring structure.



(–)-cryptaustoline (1) (–)-cryptowoline (2)

Figure 2

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7. ^{1}H-NMR spectra were recorded on a JEOL-JNM-GX500 spectrometers (500 MHz) in a mixture of deuteriochloroform and trifluoroacetic acid (ca. 10:1).

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