SYNTHESIS OF (±)-ROEMECARINE AND (±)-EPIROEMECARINE: REVISED STEREOSTRUCTURE FOR (+)-ROEMECARINE

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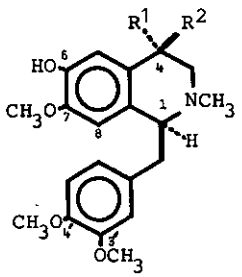
Abstract—— (±)-Roemecarine (1) and (±)-epiroemecarine (2) were synthesized from (±)-1,4-trans- and (±)-1,4-cis-4-acetoxy-1-benzyltetrahydroisoquinolin-6-ols (3 and 4). The present synthesis revealed that stereostructure of (+)-roemecarine was 1.

Recently, Shamma et al.[1] have reported that a new 4-hydroxy-1-benzyltetrahydroisoquinoline alkaloid, (+)-roemecarine, isolated from Roemeria carica A. Baytop (Papaveraceae) is 1,4-cis-4,6-dihydroxy-7-methoxy-1-(3',4'-dimethoxybenzyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (2) on the basis of the ^{1}H-nmr spectral evidence. However, the relative stereochemistry of the 1-benzyl vs. 4-hydroxyl groups seemed to be ambiguous, because the syn relationship proposed for the alkaloid is solely based on that in 4-hydroxyaporphine, which essentially differs from 1-benzyltetrahydroisoquinoline in its conformational rigidity, and from a consideration of the ^{1}H-nmr spectra[2] of 3 and 4 the up-field shifted signal due to 8-H (δ5.76) observed in the alkaloid is rather suggestive of the anti relationship. In order to clarify the ambiguity, therefore, synthesis of (±)-1 and (±)-2 was required. We now wish to report the synthesis of (±)-1 and (±)-2 and the revised stereostructure (1) for (+)-roemecarine.

Hydrolysis of 4[2] in 5% methanolic KOH solution (r.t., 2.1 h) gave (±)-1,4-cis-4,6-diol (2)[3,4]. However, the ^{1}H-nmr spectral datum of (±)-2 was inconsistent with that of the alkaloid described in the literature[1]. On the other hand, a similar hydrolysis of 3[2] (r.t., 6 h) gave (±)-1,4-trans-4,6-diol (1)[3-5], the ^{1}H-nmr spectral datum

of which was identical with that of the alkaloid described therein[1,6].

Thus, it was proved that the stereostructure of (+)-roemecarine was 1,4-trans-4,6-dihydroxy-1-(3',4'-dimethoxybenzyl)-7-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (1). Synthesis of the natural alkaloid is in progress.



	R^1	R^2
1	OH	H
2	H	OH
3	OAc	H
4	H	OAc

REFERENCES AND NOTES

1. T. Gözler, B. Gözler, N. Tanker, A. J. Freyer, H. Guinaudeau, and M. Shamma, Heterocycles, 1986, 24, 1227.
2. O. Hoshino, M. Ohtani, B. Umezawa, and Y. Iitaka, Chem. Pharm. Bull., 1984, 32, 4872.
3. All new compounds noted in the text gave satisfactory elemental analyses.
4. (±)-Roemecarine (1); mp 115.5-117°C (C_6H_6-hexane) (87%). ^{1}H-nmr δ (400 MHz) ($CDCl_3$): 2.69 (3H, s, NCH_3), 3.48 (3H, s, 7-OCH_3), 3.77, 3.86 (each 3H, s, 2 x OCH_3), 4.48 (1H, t, J=2.8 Hz, 4-H), 5.73 (1H, s, 8-H), 6.45 (1H, d, J=1.9 Hz, 2'-H), 6.54 (1H, dd, J=1.9, 8.1 Hz, 6'-H), 6.77 (1H, d, J=8.1 Hz, 5'-H), 6.95 (1H, s, 5-H). Ms m/z (%): 358 $(M-1)^+$ (0.1), 315, 208 (100), 190, 151.

   (±)-Epiroemecarine (2); mp 140-141.5°C (C_6H_6-hexane) (59%). ^{1}H-nmr δ (400 MHz) ($CDCl_3$): 2.63 (3H, s, NCH_3), 3.64 (3H, s, 7-OCH_3), 3.80 (6H, s, 2 x OCH_3), 4.33 (1H, br t, 4-H), 6.31 (1H, d, J=2.0 Hz, 2'-H), 6.53 (1H, s, 8-H), 6.54 (1H, dd, J=2.0, 8.3 Hz, 6'-H), 6.70 (1H, d, J=8.3 Hz, 5'-H), 6.81 (1H, s, 5-H). Ms m/z (%): 358 $(M-1)^+$ (0.1), 256, 208 (100), 190, 151.
5. Acetylation with Ac_2O-pyridine gave (±)-1,4-trans-4,6-diacetoxy-1-(3',4'-dimethoxybenzyl)-7-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline, ^{1}H-nmr spectrum of which was identical with that of an authentic sample[2].
6. A direct comparison of each spectrum was not carried out, because we could not have the spectrum of the alkaloid.

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