

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

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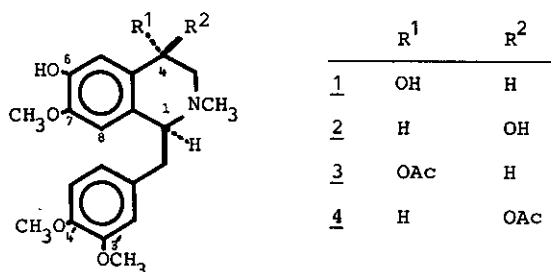
Abstract— (±)-Roemecarine (1) and (±)-epiroemecarine (2) were
synthesized from (±)-1,4-trans- and (±)-1,4-cis-4-acetoxy-1-
benzyltetrahydroisoquinolin-6-ols (3 and 4). The present synthe-
sis revealed that stereostructure of (+)-roemecarine was 1.

Recently, Shamma *et al.*¹ have reported that a new 4-hydroxy-1-benzyltetrahydroiso-
quinoline alkaloid, (+)-roemecarine, isolated from *Roemeria carica* A. Baytop (Papa-
veraceae) 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 ¹H-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-benzyltetra-
hydroisoquinoline in its conformational rigidity, and from a consideration of the
¹H-nmr spectra² 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 4² in 5% methanolic KOH solution (r.t., 2.1 h) gave (±)-1,4-cis-4,6-
diol (2)^{3,4}. However, the ¹H-nmr spectral datum of (±)-2 was inconsistent with that
of the alkaloid described in the literature¹. On the other hand, a similar hydroly-
sis of 3² (r.t., 6 h) gave (±)-1,4-trans-4,6-diol (1)³⁻⁵, the ¹H-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.



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 (C₆H₆-hexane) (87%). ¹H-nmrδ(400 MHz) (CDCl₃): 2.69(3H, s, NCH₃), 3.48(3H, s, 7-OCH₃), 3.77, 3.86(each 3H, s, 2 × OCH₃), 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 (C₆H₆-hexane) (59%). ¹H-nmrδ(400 MHz) (CDCl₃): 2.63(3H, s, NCH₃), 3.64(3H, s, 7-OCH₃), 3.80(6H, s, 2 × OCH₃), 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 Ac₂O-pyridine gave (±)-1,4-trans-4,6-diacetoxy-1-(3',4'-dimethoxybenzyl)-7-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline, ¹H-nmr spectrum of which was identical with that of an authentic sample².
6. A direct comparison of each spectrum was not carried out, because we could not have the spectrum of the alkaloid.

Received, 8th May, 1987