

Short Communications

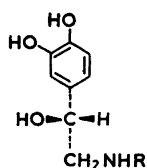
The Absolute Configuration of the Cactus Alkaloid (—)-Calipamine *

RONALD W. WOODARD,^a J. CYMERMAN CRAIG^a and JAN G. BRUHN^{b,**}^a Department of Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, California 94143 and ^b Department of Pharmacognosy, Faculty of Pharmacy, Biomedium, Box 579, S-751 23 Uppsala, Sweden

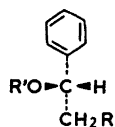
The alkaloid (—)-calipamine was isolated from *Coryphantha calipensis* H. Bravo¹ and shown to consist of one optical isomer. From NMR spectra, alkaline permanganate oxidation, and acid hydrolysis, calipamine was deduced¹ to have the structure *N*-methyl-3,4-dimethoxy- β -methoxyphenethylamine **1**. The natural alkaloid must, therefore, have the absolute configuration shown in **1** or its mirror image.



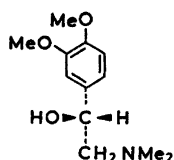
1. R = H
6. R = CH₃



2. R = H
5. R = CH₃



3. R = OH R' = H
4. R = H R' = H
5. R = H R' = CH₃



7.

The circular dichroism (CD) curve for (—)-calipamine hydrochloride showed a positive

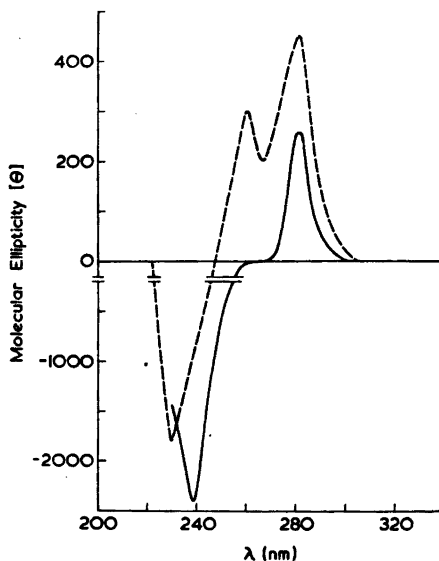


Fig. 1. Circular dichroism spectra of (—)-calipamine hydrochloride (—) and *R*-(-)-noradrenaline hydrochloride (- - -).

Cotton effect centered at 281 nm and a strong negative one centered at 239 nm. The compound (*R*-(-)-noradrenaline hydrochloride **2**, with an identical carbon skeleton and nitrogen and oxygen substitution pattern, had a very similar CD spectrum (Table 1). Since the nitrogen $n \rightarrow \sigma^*$ transition in both **1** and **2** has been abolished by protonation, the observed CD maxima correspond to the 1L_b and 1L_a transitions, respectively, of the benzene chromophore, asymmetrically perturbed by the center of asymmetry adjacent to the ring. As is usual when oxygen substitution is present in positions 3 and 4, the 1L_b transition is shifted from 260 to 280 nm, while the 1L_a transition is moved to 235 nm from 210 nm, both shifts being accompanied by a loss of fine structure. This wavelength shift is due to an overlap of the π orbital of benzene with the nonbonding p orbital of the oxygen substituents in the ring.²

This was confirmed by the CD spectra of *R*-(-)-1-phenylethane-1,2-diol **3** and *S*-(-)-1-phenylethanol **4** (Table 1) which showed superimposable maxima centered at 268 (positive c.e.) and 216 nm (negative c.e.), with the normal

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** Present address: Department of Toxicology, Karolinska Institute, S-104 01 Stockholm, Sweden.

Table 1. CD spectra and rotations.

Compound	CD maxima [θ] (nm) ^a				[α] _D ²⁵ (°)			
	¹ L _b	Band	¹ L _a	Band	in 95 % ethanol			
<i>S</i> -(-)-Phenylethanol 4 (<i>D</i>)	260 (267)	300 (260)	208 (255)	130 (249)	-1561 (218)	-2342 (215)	-2863 (213)	-39.1 (c 1.92)
<i>S</i> -(-)-1-Methoxy-1-phenylethane 5 (<i>D</i>)	246 (268)	220 (240)	163 (254)	79 (249)		-352 (216) ^c		-119.2 (c 1.02)
<i>R</i> -(-)-Phenylethane-1,2-diol 3 (<i>D</i>)	178 (268)	193 (261)	131 (255)	92 (249)		-620 (218) ^c		-40.0 (c 0.294)
<i>R</i> -(-)-Noradrenaline HCl 2 (<i>D</i>)	449 (281)	300 (260)				-1795 (230)		-40.0 (c 0.034)
(-)-Calipamine·HCl 1	260 (281)					-2392 (239)		-91.7 (c 0.01) ^b

^a In 95 % ethanol. ^b In absolute ethanol. ^c Lowest wavelength reached.

fine structure for both transitions. The weak $n \rightarrow \sigma^*$ transition of the additional OH group in 3 thus does not change the nature of the CD spectrum compared to 4. Further, methylation³ of the OH group in 4 (silver oxide/methyl iodide) gave *S*-(-)-1-methoxy-1-phenyl-

ethane 5 with an almost identical CD spectrum (Table 1), indicating the lack of effect of the change OH \rightarrow OCH₃ at the asymmetric center.

Since compounds 2–5 all possess the identical (*D*) configuration,⁴ this also indicates the asymmetric center in (-)-calipamine to have the configuration shown in 1, i.e. (*R*). As (-)-1 was converted (formaldehyde/sodium borohydride) to (-)-*N,N*-dimethyl-3,4-dimethoxy- β -methoxyphenethylamine identical with the natural product 6 found in the same plant,¹ it follows that the natural *N,N*-dimethyl derivative 6 also has the (*R*)-configuration. It is interesting that the closely related cactus alkaloid (-)-macromerine 7 was recently shown⁶ to have the (*R*)-configuration by chemical correlation with natural (*R*)-adrenaline 8.

Experimental. CD curves were measured with a Jouan Mark II spectropolarimeter at 25 °C in 95 % ethanol, and were recorded in terms of molecular ellipticity units [θ].⁵ Only CD maxima are given.

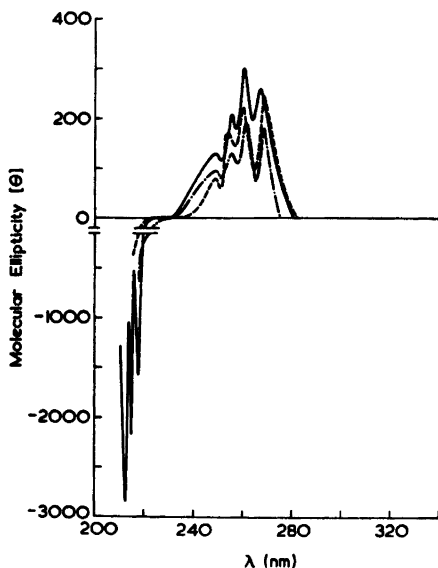


Fig. 2. Circular dichroism spectra of *R*-(-)-1-phenylethane-1,2-diol (---), *S*-(-)-1-phenylethanol (—), and *S*-(-)-1-methoxy-1-phenylethane (· · ·).

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2. Moffitt, W. *J. Chem. Phys.* 22 (1954) 320; Petruska, J. *J. Chem. Phys.* 34 (1961) 1111.
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4. Note, however, that the changing priority requirements of the sequence rule cause a change from the (*R*)- to the (*S*)-designation.
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