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CONFIGURATION OF THE RING *A* METHOXYL IN DELPHININE AND ACONITINE

Karin Bjåmer Birnbaum

Biochemistry Laboratory, National Research Council, Ottawa, Canada

and

K. Wiesner, E.W.K. Jay and Lizzie Jay (Poon)

Natural Products Research Center, University of New Brunswick

Fredericton, New Brunswick, Canada

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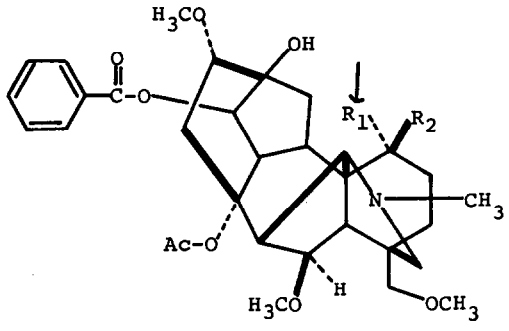
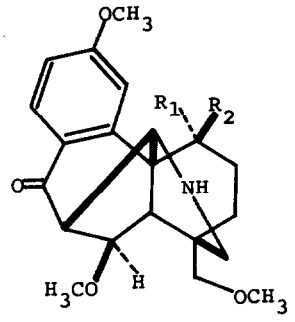
Eleven years ago the structure (1) was deduced[1] for the alkaloid delphinine. The configuration (1) of the ring *A* methoxyl in delphinine (marked by the arrow) was assigned[2] on the basis of a direct correlation[3] of delphinine with aconitine, in the course of which this asymmetric center remained undisturbed. The corresponding ring *A* methoxyl of aconitine in turn was assigned the configuration *trans* to the nitrogen bridge on the basis of a conformational argument[4]. A similar conformational argument seemed also to hold when this substituent was studied directly in delphinine[2]. It will be shown in the present communication that the configuration of the ring *A* methoxyl in aconitine and delphinine has to be reversed and thus delphinine has to be represented by (2). The erroneous result of the conformational arguments mentioned seems to reflect the basic uncertainty about the conformation of ring *A* in alkaloids of the delphinine type. Delphinine may be readily degraded to an aromatization product formulated (if we discard the conformational argument quoted above) as (3) or (4)[5]. We have recently synthesized stereoselectively both epimers (3) and (4) and have shown that one of the two racemates is clearly identical with the optically active

degradation product of delphinine while the other one is clearly different[6]. Moreover, we have resolved the "identical racemate" into optical antipodes and have shown that the totally synthetic optically active product is identical with the "natural" degradation product by mixed melting points, rotatory dispersion and all spectral criteria[7]. Since the synthesis, in spite of its stereoselectivity, did not provide a possibility to assign the configuration of the ring *A* methoxyl we have decided to determine this configuration in the "identical racemate", in the form of its acid oxalate (m.p. 189-192°), by X-ray crystallography.

We have chosen the racemate rather than the optically active compound since we feel that long laborious total syntheses are practically immune to the healthy process of independent verification and that an X-ray structure determination of the racemate may fulfill also this objective.





(1) $R_1 = OCH_3$; $R_2 = H$

(2) $R_1 = H$; $R_2 = OCH_3$

(3) $R_1 = OCH_3$; $R_2 = H$

(4) $R_1 = H$; $R_2 = OCH_3$

The crystals of the acid oxalate, $C_{22}H_{30}O_5N \cdot C_2HO_4$, are monoclinic and there are eight ion pairs in a unit cell of dimensions a = 23.972, b = 10.346, c = 18.656Å; β = 93.16°. From the systematic absences the space group could be either Cc (non-centrosymmetric) or C2/c (centrosymmetric). The data were collected on a Picker automatic diffractometer using CuKα radiation and of the 3921 accessible reflections ($2\theta \leq 130°$) 3120 were observed. The statistics of the normalized structure factors (E's) showed clearly that the space group was

centrosymmetric, *i.e.* C2/c.

The structure was solved by the symbolic-addition procedure[8] using 382 terms with $|E| \geq 1.65$. The following six starting reflections were used:

h	k	ℓ	|E|	sign
16,	2,	7	4.19	+
11,	11,	0	3.20	+
-21,	1,	11	4.20	-
-18,	4,	4	2.92	-
-21,	3,	7	2.83	+
10,	8,	4	2.80	-

The first two reflections define the origin and their signs were chosen to be positive and all sixteen possible combinations of signs for the other four were tried. The set of signs shown above resulted in the largest number of signs deduced for other reflections and in fewest contradictions in the determination of the symbols. Another indication that this set of signs was correct was that the Karles' R factor[8] had the low value of 16.5%. An E-map was calculated with

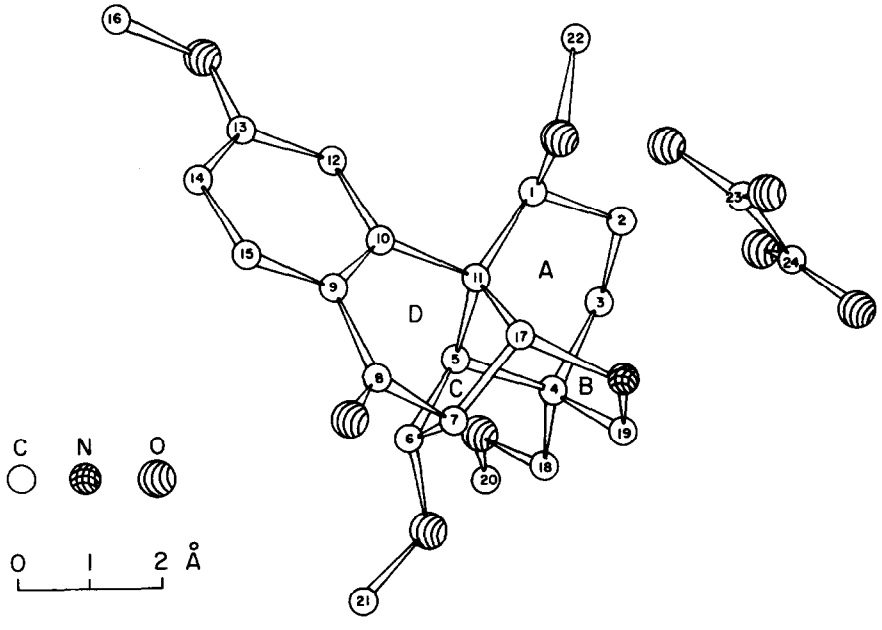


Figure. View of the ion pair along the c*-axis

these terms and all 34 non-hydrogen atoms were located from it. The hydrogen atoms were found from a difference Fourier map. The parameters have been refined by least squares and the present R factor is 5.7% for all observed reflections. The refinement is being continued.

A perspective view of the molecule can be seen in the Figure. Ring *A* occurs in the chair conformation and the methoxyl group at C(1) is equatorial. The "identical" synthetic racemate has thus been shown to possess the configuration (4) and consequently delphinine must have the configuration (2). Ring *B* is also a chair, the five-membered ring *C* occurs in the envelope conformation and ring *D* is a distorted half-chair. Each hydrogen atom attached to the nitrogen is hydrogen bonded to an oxygen atom in two different oxalate ions, the N---O lengths being 2.71 and 2.75Å.

Complete results of the X-ray analysis will be published (by K.B.B.) elsewhere.

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