Table 4. *Condensed references to derivatives of 1,2,4-trioxane and 1,2-dioxane retrieved from the Cambridge Structural Database (CSD)*

CSD Refcode	Conf.[a]	Fused[b]	Coden	Vol.	Page	Year
(*a*) 1,2,4-Trioxane						
BHSPXD	C	*t*	JACSAT	96	2955	1974
COBMUB	C	*c*	HCACAV	67	1104	1984
IMNATX10	C	*n*	ACBCAR	33	3564	1977
Compound *A*[c]	C	*c*	HCACAV	67	2254	1984
Compound *B*[c]	C	*n*	TETRAB	41	2081	1985
(I)	C	*c*	This work			
QNGHSU	TB	*t*	SSBSEF	23	380	1980
(II)	TB	*c*	This work			
(*b*) 1,2-Dioxane						
BOJTUP	C	*n*	JCPKBH	–	1523	1982
BUDYII	C	*n*	JACSAT	105	1199	1983
OXBCHA	C	*n*	JACSAT	102	7574	1980
OXBCHB	C	*n*	JACSAT	102	7574	1980

(*a*) Conformation: C = chair, TB = twist boat.
(*b*) Fusion geometry: *c* = *cis*, *t* = *trans*, *n* = none.
(*c*) Structures not yet in CSD on 1 May 1985.

The twist-boat conformation adopted by the 1,2,4-trioxane in (II) is a result of geometrical constraints imposed by the *cis*-fused cyclopentene ring. The only other twist-boat 1,2,4-trioxane is in the antimalarial *Qinghaosu* (ASQRG, 1980). Here, however, the trioxane is part of a more complex bridged and fused ring assembly; the O—O torsion angle is low at 47·4° [84·6 (4)° in (II)] whilst the maximum angle of 75·1° is associated with O(2)—C(3).

The O—O bond lengths in (I) [1·467 (1) Å] and (II) [1·469 (2) Å] may be regarded as identical and are in excellent agreement with the mean value of 1·470 (2) Å for 43 cyclic Csp^3—O—O—Csp^3 fragments in structures with $R < 0{\cdot}07$ obtained from CSD (Allen *et al.*, 1979). The C—O distances in (I) and (II), however, show a wide range [1·401 (1)–1·444 (1) Å]. This is typical of the trioxanes of Table 4(*a*) where the C—O bonds range from 1·393 (18) to 1·466 (16) Å. Variability of C—O bond lengths has been discussed by Allen & Kirby (1984); in the current examples such distances will be heavily dependent on the electronic nature of the ring substituents.

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Structure of Synthetic (±)-Gephyrotoxin-223AB Hydrobromide*

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Abstract. 3-*n*-Butyl-5-*n*-propylperhydroindolizine hydrobromide, $C_{15}H_{30}N^+.Br^-$, $M_r = 304{\cdot}33$, monoclinic, $P2_1/c$, $a = 19{\cdot}299$ (4), $b = 12{\cdot}921$ (2), $c = 14{\cdot}263$ (3) Å, $\beta = 110{\cdot}86$ (1)°, $V = 3323{\cdot}5$ Å^3, $Z = 8$ with two molecules per asymmetric unit, $D_m = 1{\cdot}220$, $D_x = 1{\cdot}216$ Mg m^{-3}, $\lambda(\text{Cu } K\alpha_1) = 1{\cdot}54056$ Å, $\mu = 3{\cdot}23$ mm^{-1}, $F(000) = 1296$, $T = 297$ K. $R = 0{\cdot}046$ for 3843 observed reflexions. The five-membered ring is in the N-envelope form, the six-membered ring has the chair conformation, and the ring junction is *trans*. The side chains in the two independent molecules show some significant conformational differences. Hydrogen bonds of the type N—H···Br···H—C link the molecules into chains parallel to **c**.

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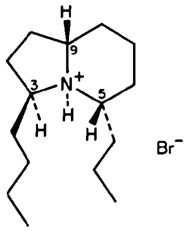
Introduction. The potent neurotoxic secretions of the skins of South American *Dendrobates* frogs contain many alkaloids. A synthesis of one of these, gephyrotoxin-223AB, carried out in the laboratory of O. E. Edwards, was based on pseudo Diels–Alder reaction of *N*-acylimmonium salts (Edwards, Greaves & Sy, 1984, unpublished work). The relative stereochemistry at C(5) and C(9) was assigned from ^{1}H NMR studies, but the configuration at C(3) in the major product was uncertain. The synthetic compound proved identical to the natural product (Spande, 1984) except for the lack of optical activity. However, the stereochemistry suggested for the natural material had not been established unequivocally (Spande, Daly, Hart, Tsai & Macdonald, 1981; Macdonald, 1980). This analysis of the synthetic (±)-toxin hydrobromide confirms the relative stereochemistry as shown in (I).



(I)

Experimental. Crystals obtained from ethyl acetate, density measured by flotation in toluene and carbon tetrachloride mixture. X-ray measurements carried out with a crystal 0·22 × 0·26 × 0·26 mm, on an Enraf–Nonius CAD-4 diffractometer with Ni-filtered Cu radiation. Unit-cell parameters derived from θ values of 18 reflexions with $35 < \theta < 42°$, by a least-squares fit restricting α and γ to 90°. Intensities measured by ω–2θ scans with $\Delta\omega = (0{\cdot}8 + 0{\cdot}35\tan\theta)°$, extended by 25% at each end for the background. Three standard reflexions measured every hour showed random variations within 5% and a steady decrease amounting to 14% throughout the experiment. Data collected to $\theta_{\max} = 65°$ for $h = -21$ to 21, $k = 0$ to 15 and $l = 0$ to 16. Of the 5656 reflexions measured, 3843 observed with $I \geq 3\sigma(I)$. Data corrected for scale variation and Lp effects but not for absorption, which was estimated to be in the range 2·04 to 2·33.

Structure determined by direct methods with *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978) and refined by block-diagonal least squares, 9 × 9 per atom (4 × 4 for H), minimizing $\sum w(|F_o| - |F_c|)^2$ with $w = 1/[1 + (|F_o|/25)^2]$. The parameters for nine H atoms of the side chains in molecule (II) did not refine satisfactorily and were therefore fixed. In final cycle, $R = 0{\cdot}046$ for observed reflexions, $wR = 0{\cdot}064$, $S = 1{\cdot}01$, average shift = $0{\cdot}04\sigma$ and max. shift = $0{\cdot}34\sigma$. Residual electron density in final difference map within $\pm 0{\cdot}56$ e Å^{-3}, with most of the highest peaks associated with the Br atoms.

Table 1. *Fractional coordinates* (× 10^5 *for* Br, × 10^4 *for* C *and* N) *with e.s.d's in parentheses and equivalent isotropic temperature factors* (Å^2)

$$B_{\rm eq} = \tfrac{8}{3}\pi^2 \textstyle\sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i . \mathbf{a}_j.$$

	x	y	z	$B_{\rm eq}$
Molecule (I)				
Br(1)	7825 (3)	14063 (4)	38625 (3)	6·3
C(1)	−40 (3)	3431 (4)	5162 (4)	6·5
C(2)	−585 (3)	2531 (4)	5000 (4)	6·4
C(3)	−198 (2)	1700 (3)	5768 (3)	4·7
N(4)	614 (2)	1968 (3)	5998 (2)	4·4
C(5)	1198 (2)	1449 (4)	6860 (3)	5·0
C(6)	1950 (2)	1850 (5)	6886 (3)	6·4
C(7)	2003 (3)	3010 (5)	6935 (4)	7·3
C(8)	1388 (3)	3510 (4)	6063 (4)	6·5
C(9)	648 (2)	3124 (4)	6052 (3)	5·4
C(10)	−392 (2)	1677 (3)	6709 (3)	5·1
C(11)	−1208 (2)	1424 (4)	6474 (3)	5·6
C(12)	−1377 (3)	1181 (5)	7401 (4)	7·3
C(13)	−2190 (3)	964 (6)	7192 (5)	9·8
C(14)	1138 (2)	278 (4)	6759 (3)	5·9
C(15)	1614 (3)	−307 (5)	7692 (5)	8·9
C(16)	1360 (5)	−203 (7)	8557 (5)	12·4
Molecule (II)				
Br(2)	42084 (3)	14898 (4)	80156 (3)	6·7
C(101)	5100 (3)	3531 (4)	10098 (4)	6·4
C(102)	5614 (3)	2627 (4)	10402 (4)	6·6
C(103)	5241 (2)	1791 (3)	10795 (3)	4·6
N(104)	4433 (2)	2088 (3)	10301 (2)	4·2
C(105)	3852 (2)	1570 (3)	10625 (3)	4·9
C(106)	3106 (2)	2029 (5)	9989 (3)	6·3
C(107)	3081 (3)	3191 (5)	10023 (3)	6·6
C(108)	3678 (3)	3659 (4)	9702 (3)	6·3
C(109)	4424 (2)	3249 (3)	10360 (3)	4·9
C(110)	5473 (2)	1711 (3)	11926 (3)	5·1
C(111)	6276 (3)	1408 (4)	12424 (4)	6·1
C(112)	6466 (3)	1166 (5)	13550 (4)	8·0
C(113)	7253 (4)	902 (8)	14055 (5)	11·6
C(114)	3892 (3)	407 (4)	10547 (3)	6·1
C(115)	3465 (3)	−164 (5)	11100 (5)	8·4
C(116)	3867 (4)	−126 (7)	12219 (6)	11·4

Scattering factors from *International Tables for X-ray Crystallography* (1974) and Stewart, Davidson & Simpson (1965). Computations made with the aid of the *NRC* program system (Ahmed, Hall, Pippy & Huber, 1973). The refined atomic parameters for molecules (I) and (II) are listed in Table 1.*

Discussion. Molecules (I) and (II) of the asymmetric unit have been arbitrarily chosen with opposite configurations. The stereochemistry of molecule (I) (Fig. 1) is 3*S*,5*S*,9*S*, whereas that of molecule (II) is 3*R*,5*R*,9*R*. Recently, Royer & Husson (1985) published the details of an enantiospecific synthesis of the natural 3*R*,5*R*,9*R*-(−)-gephyrotoxin-223AB, thus establishing that enantiomer (II) of the title compound represents the absolute configuration of the natural product. It should be noted that gephyrotoxin-223AB is not closely related to gephyrotoxin whose structure and absolute configuration were determined crystallographically by Daly, Witkop, Tokuyama, Nishikawa & Karle (1977).

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* Lists of observed and calculated structure amplitudes, anisotropic thermal parameters and H parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42797 (28 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

The bond lengths and valence angles for both enantiomers, not corrected for thermal vibration, are presented in Table 2. Most of the equivalent values agree within experimental error. The C—N bond lengths vary from 1·496 (7) to 1·522 (6) Å with a mean value of 1·508 Å. Equivalent torsional angles of the rings are similar in the two molecules, while the values for the side chains show significant conformational differences as shown in Table 3.

The ring junction is *trans* and the propyl group is equatorial. The six-membered rings have slightly flattened chair conformations, as their torsional angles vary from 54·0 (5) to 59·5 (5)° with an average value of 56·6°. The five-membered rings have envelope conformations with asymmetry parameters $\Delta C_s(N)$ of 2·9 and 3·3° for (I) and (II), respectively (Duax, Weeks & Rohrer, 1976). The C(9)—C(1)—C(2)—C(3) torsional angles in (I) and (II) are −2·1 (5) and 2·7 (6)° respectively, and the distance of N(4) from the mean plane through those four atoms is 0·621 (4) Å in (I) and 0·618 (3) Å in (II). In another perhydroindolizine dendrobatid alkaloid where the five-membered ring is without any substituents at C(3), the ring assumes a half-chair conformation (Daly, Tokuyama, Fujiwara, Highet & Karle, 1980).

The H atoms attached to N(4) in (I) and N(104) in (II) form hydrogen bonds to their closest Br(1) and Br(2) atoms respectively, with N–H = 0·71 (3), 0·75 (4) Å; H···Br = 2·57 (3), 2·48 (4) Å; N–H···Br = 168 (3), 173 (4)° for molecules (I) and (II), respectively. In addition, the inductive effects of positively charged N atoms appear to allow the formation of weak C(9′)—H···Br(1) and C(109′)—H···Br(2) bonds (Taylor & Kennard, 1982) so that the molecules are linked by N—H···Br···H—C hydrogen bonds into chains parallel to **c**. These bonds have C—H = 1·02 (4) and 0·98 (4) Å, H···Br = 3·01 (4) and 3·02 (4) Å, C—H···Br = 161 (3) and 158 (3)° for molecules (I) and (II) respectively.

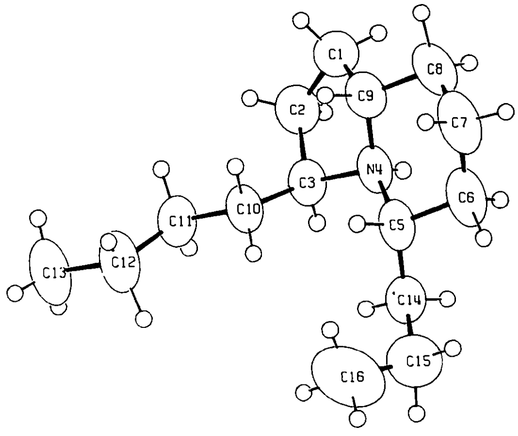

Fig. 1. *ORTEP*II (Johnson, 1971) projection of the cation (I) showing 50% probability thermal ellipsoids and the atom-numbering scheme.

Table 2. *Bond lengths* (Å) *and angles* (°)

	(I)	(II)		(I)	(II)
C(1)—C(2)	1·529 (8)	1·493 (8)	C(6)—C(7)	1·502 (9)	1·504 (9)
C(1)—C(9)	1·527 (7)	1·524 (7)	C(7)—C(8)	1·524 (8)	1·509 (8)
C(2)—C(3)	1·526 (7)	1·512 (7)	C(8)—C(9)	1·508 (7)	1·507 (7)
C(3)—N(4)	1·522 (6)	1·514 (6)	C(10)—C(11)	1·524 (6)	1·508 (7)
C(3)—C(10)	1·517 (6)	1·516 (6)	C(11)—C(12)	1·503 (7)	1·547 (8)
N(4)—C(5)	1·498 (5)	1·513 (6)	C(12)—C(13)	1·515 (9)	1·471 (10)
N(4)—C(9)	1·496 (7)	1·503 (6)	C(14)—C(15)	1·522 (8)	1·519 (8)
C(5)—C(6)	1·529 (6)	1·522 (6)	C(15)—C(16)	1·487 (10)	1·507 (10)
C(5)—C(14)	1·520 (7)	1·511 (7)			
C(2)—C(1)—C(9)	106·0 (4)	106·3 (4)	C(5)—C(6)—C(7)	112·8 (4)	113·8 (4)
C(1)—C(2)—C(3)	107·0 (4)	108·2 (4)	C(6)—C(7)—C(8)	111·4 (5)	110·7 (4)
C(2)—C(3)—N(4)	101·4 (3)	101·2 (3)	C(7)—C(8)—C(9)	109·1 (4)	109·5 (4)
C(2)—C(3)—C(10)	115·9 (4)	116·4 (4)	C(1)—C(9)—N(4)	102·0 (4)	101·4 (3)
N(4)—C(3)—C(10)	111·9 (3)	112·2 (3)	C(1)—C(9)—C(8)	117·6 (4)	118·3 (4)
C(3)—N(4)—C(5)	119·4 (3)	119·9 (3)	N(4)—C(9)—C(8)	110·8 (4)	110·1 (3)
C(3)—N(4)—C(9)	105·1 (3)	104·9 (3)	C(3)—C(10)—C(11)	111·8 (3)	112·5 (4)
C(5)—N(4)—C(9)	113·5 (3)	113·6 (3)	C(10)—C(11)—C(12)	112·5 (4)	111·4 (4)
N(4)—C(5)—C(6)	107·4 (4)	107·0 (3)	C(11)—C(12)—C(13)	113·5 (5)	112·2 (5)
N(4)—C(5)—C(14)	111·0 (4)	110·8 (3)	C(5)—C(14)—C(15)	114·2 (4)	113·2 (4)
C(6)—C(5)—C(14)	112·3 (4)	114·0 (4)	C(14)—C(15)—C(16)	114·0 (6)	111·4 (6)

Table 3. *Torsional angles* (°) *of the side chains, with e.s.d.'s in parentheses*

	(I)	(II)
Propyl chain		
C(6)—C(5)—C(14)—C(15)	70·6 (5)	−73·8 (5)
C(5)—C(14)—C(15)—C(16)	69·0 (7)	−74·2 (6)
Butyl chain		
C(2)—C(3)—C(10)—C(11)	63·5 (5)	−64·6 (5)
C(3)—C(10)—C(11)—C(12)	168·1 (4)	−171·1 (4)
C(10)—C(11)—C(12)—C(13)	177·9 (5)	−178·1 (5)

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