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THE CRYSTAL AND MOLECULAR STRUCTURE OF HETISINE PERCHLORATE

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ABSTRACT.—Hetisine perchlorate crystallizes in the monoclinic space group $P2_1$ with two molecules of alkaloid and two perchlorate ions in the asymmetric unit. The structure was solved by multisolution methods and refined to an R of 0.069 for 4004 observed reflections.

A rearrangement product (1) of hetisine has configurations of the hydroxyl groups at C11 and C13 opposite to those determined for hetisine hydrobromide (2). We questioned whether the reversal of the configuration occurred during the rearrangement or whether hetisine itself had a configuration different from what had been reported previously. Because an error in the X-ray structure assigned to the hydroiodide salt of 4-de(oxymethylene)lycoctonine (3) has been demonstrated recently by new X-ray analyses on lycoctonine transformation products (4, 5) and by X-ray analyses of browniine perchlorate and dictyocarpine (6), we decided to carry out a new X-ray structure determination on hetisine perchorate after establishing the homogeneity of our sample of hetisine by nmr studies.

This investigation confirmed the structure and stereochemistry of hetisine to be **1** as established earlier (2), clearing the way for understanding the pathway of the rearrangement reaction (1). The bond lengths and angles of the two hetisine molecules are listed in Tables 1 and 2. The standard deviations in bond lengths vary from 0.004 to 0.007 Å and those in bond angles vary from 0.4 to 0.6°. As the second perchlorate is disordered, the positions of the oxygens attached to Cl2 are not as accurate as the coordinates of other atoms.

The conformations of the molecules are shown in Figure 1.

TABLE 1. Bond Lengths (Å)[a] for Hetisine Perchlorate

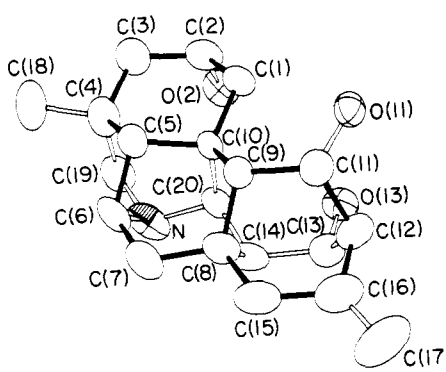
	Mol-A	Mol-B		Mol-A	Mol-B
O(2)-C(2)	1.447	1.417	C(6)-C(7)	1.505	1.514
O(11)-C(11)	1.432	1.408	C(7)-C(8)	1.518	1.516
O(13)-C(13)	1.421	1.422	C(8)-C(9)	1.530	1.541
N-C(6)	1.538	1.495	C(8)-C(14)	1.550	1.563
N-C(19)	1.532	1.508	C(8)-C(15)	1.562	1.535
N-C(20)	1.509	1.520	C(9)-C(10)	1.569	1.565
C(1)-C(2)	1.504	1.519	C(9)-C(11)	1.562	1.539
C(1)-C(10)	1.523	1.514	C(10)-C)20)	1.553	1.566
C(2)-C(3)	1.520	1.495	C(11)-C(12)	1.548	1.564
C(3)-C(4)	1.500	1.534	C(12)-C(13)	1.545	1.530
C(4)-C(5)	1.542	1.531	C(12)-C(16)	1.525	1.521
C(4)-C(18)	1.576	1.559	C(13)-C(14)	1.553	1.556
C(4)-C(19)	1.508	1.528	C(14)-C(20)	1.510	1.533
C(5)-C(6)	1.523	1.534	C(15)-C(16)	1.480	1.504
C(5)-C(10)	1.564	1.562	C(16)-C(17)	1.332	1.340

[a]Standard deviations vary from 0.004 to 0.007.

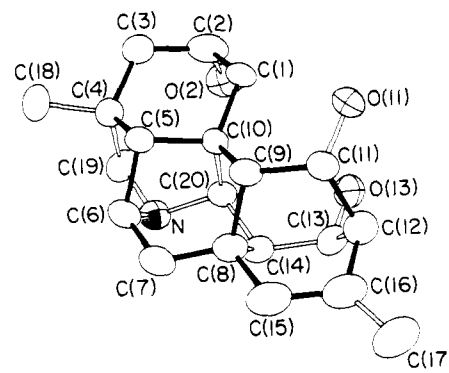
TABLE 2. Bond Angles (DEG)[a] for Hetisine Perchlorate

	Mol-A	Mol-B		Mol-A	Mol-B
C(6)-N-C(19)	102.5	103.4	C(8)-C(9)-C(11)	106.8	107.4
C(6)-N-C(20)	102.9	103.5	C(10)-C(9)-C(11)	122.4	122.4
C(19)-N-C(20)	110.3	110.2	C(1)-C(10)-C(5)	110.9	112.1
C(2)-C(1)-C(10)	116.8	115.4	C(1)-C(10)-C(9)	117.0	116.7
O(2)-C-(2)-C(1)	112.1	109.3	C(1)-C(10)-C(20)	116.3	113.9
O(2)-C(2)-C(3)	108.6	112.2	C(5)-C(10)-C(9)	106.2	107.2
C(1)-C(2)-C(3)	110.6	112.5	C(5)-C(10)-C(20)	102.2	101.2
C(2)-C(3)-C(4)	116.2	115.5	C(9)-C(10)-C(20)	102.7	104.2
C(3)-C(4)-C(5)	110.1	111.5	O(11)-C(11)-C(9)	116.4	112.6
C(3)-C(4)-C(18)	105.6	106.4	O(11)-C(11)-C(12)	108.6	113.8
C(3)-C(4)-C(19)	116.6	114.4	C(9)-C(11)-C(12)	110.9	109.3
C(5)-C(4)-C(18)	110.3	111.4	C(11)-C(12)-C(13)	110.9	113.1
C(5)-C(4)-C(19)	102.8	101.7	C(11)-C(12)-C)16)	105.7	106.0
C(18)-C(4)-C(19)	111.5	111.6	C(13)-C(12)-C(16)	105.4	105.6
C(4)-C(5)-C(6)	101.8	102.0	O(13)-C(13)-C(12)	112.9	108.9
C(4)-C(5)-C(10)	110.1	111.4	O(13)-C(13)-C(14)	109.9	114.5
C(6)-C(5)-C(10)	101.4	100.9	C(12)-C(13)-C(14)	109.8	108.7
N-C(6)-C(5)	92.0	92.3	C(8)-C(14)-C(13)	110.9	110.7
N-C(6)-C(7)	109.8	111.6	C(8)-C(14)-C(20)	100.2	100.4
C(5)-C(6)-C(7)	116.8	116.3	C(13)-C(14)-C(20)	112.3	112.0
C(6)-C(7)-C(8)	111.4	111.2	C(8)-C(15)-C(16)	110.9	109.7
C-(7)-C(8)-C(9)	111.2	111.1	C(12)-C(16)-C(15)	112.4	111.6
C(7)-C(8)-C(14)	109.7	109.3	C(12)-C(16)-C(17)	123.7	122.8
C(7)-C(8)-C(15)	111.9	111.3	C(15)-C(16)-C(17)	124.0	125.6
C(9)-C(8)-C(14)	98.7	99.0	N-C(19)-C(4)	103.3	103.2
C(9)-C(8)-C(15)	114.2	113.5	N-C(20)-C(10)	102.1	101.9
C(14)-C(8)-C(15)	110.3	111.9	N-C(20)-C(14)	108.5	107.7
C(8)-C(9)-C(10)	101.4	101.1	C(10)-C(20)-C(14)	106.8	105.4

[a]Standard deviations vary from 0.4 to 0.6°.



Molecule "A"



Molecule "B"

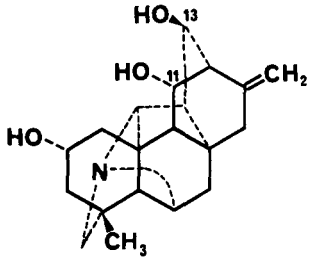
FIGURE 1. ORTEP drawings for the hetisine perchlorate molecues A and B.

TABLE 3. Coordinates and Thermal Parameters for Nonhydrogen Atoms in Hetisine Perchlorate[a]

N	Code	X/A	Y/B	Z/C	Beq
1.	CL1	3449(1)	2008(1)	3786(1)	4.6
2.	CL2	6424(1)	792(2)	1343(1)	6.5
3.	O1L1	4128(3)	1517(4)	3209(2)	6.9
4.	O2L1	3441(4)	983(4)	4336(2)	7.8
5.	O3L1	4020(5)	3255(5)	4032(3)	11.3
6.	O4L1	2264(3)	2272(6)	3547(4)	12.4
7.	O1L2	5731(4)	910(4)	1920(2)	8.3
8.	O2L2	6179(7)	1684(6)	787(3)	10.7
9.	O3L2	7407(5)	77(10)	1390(5)	14.9
10.	O4L2	6020(29)	−645(15)	1070(7)	27.6
11.	C2A	−587(2)	1916(4)	686(2)	6.4
12.	C11A	1044(2)	4411(3)	2831(1)	5.0
13.	O13A	−178(2)	5833(3)	1479(1)	5.5
14.	NA	2080(3)	3911(4)	136(1)	5.4
15.	C1A	895(2)	2395(3)	1670(1)	4.0
16.	C2A	304(3)	1302(4)	1185(2)	5.1
17.	C3A	1243(4)	537(4)	769(2)	6.3
18.	C4A	2132(3)	1453(4)	412(2)	5.4
19.	C5A	2786(3)	2434(3)	963(2)	4.4
20.	C6A	3328(3)	3539(5)	486(2)	5.4
21.	C7A	3876(3)	4823(5)	849(2)	5.5
22.	C8A	3037(3)	5452(3)	1376(2)	4.6
23.	C9A	2594(2)	4324(3)	1883(1)	3.8
24.	C10A	1843(2)	3336(3)	1354(1)	3.6
25.	C11A	2011(3)	5122(3)	2504(2)	4.5
26.	C12A	1566(4)	6605(4)	2262(2)	5.7
27.	C13A	951(3)	6547(3)	1504(2)	5.0
28.	C14A	1809(3)	5831(4)	987(2)	4.9
29.	C15A	3599(4)	6782(4)	1759(2)	6.3
30.	C16A	2704(4)	7489(4)	2194(2)	6.6
31.	C17A	2866(7)	8762(5)	2487(5)	10.5
32.	C18A	3060(5)	404(7)	88(3)	8.8
33.	C19A	1619(4)	2476(5)	−139(2)	6.1
34.	C20A	1380(3)	4376(4)	761(1)	4.2
35.	O2B	9691(3)	1239(4)	3272(2)	6.6
36.	O11B	9562(2)	−3779(3)	3581(2)	5.9
37.	O13B	8424(2)	−2109(3)	2256(1)	5.3
38.	NB	6551(2)	479(3)	3641(1)	4.2
39.	C1B	9499(2)	−924(3)	3917(2)	4.3
40.	C2B	9909(3)	607(4)	3951(2)	5.3
41.	C3B	9341(3)	1419(4)	4527(2)	5.3
42.	C4B	7969(3)	1240(3)	4559(2)	4.6
43.	C5B	7608(2)	−320(3)	4570(2)	4.0
44.	C6B	6270(3)	−260(3)	4314(2)	4.5
45.	C7B	5654(3)	−1666(4)	4166(2)	4.6
46.	C8B	6395(3)	−2589(3)	3695(2)	4.2
47.	C9B	7710(2)	−2720(3)	3999(2)	3.8
48.	C10B	8150(2)	−1153(3)	3946(1)	3.4
49.	C11B	8301(3)	−3937(3)	3603(2)	4.8
50.	C12B	7637(3)	−4126(3)	2853(2)	5.1
51.	C13B	7336(3)	−2722(3)	2481(2)	4.6
52.	C14B	6627(3)	−1778(3)	2992(2)	4.1
53.	C15B	5777(4)	−4019(4)	3547(2)	5.9
54.	C16B	6424(4)	−4802(3)	2985(2)	5.8
55.	C17B	5984(5)	−5911(5)	2611(3)	7.7
56.	C18B	7608(4)	2018(5)	5247(3)	6.9
57.	C19B	7239(3)	1772(4)	3900(2)	5.3
58.	C20B	7393(2)	−541(3)	3289(1)	3.7

[a]The fractional coordinates are multiplies by 10^4.

$$Beq = \frac{8\pi^2}{3}\left[\frac{U_{11}}{Sin^2\beta} + U_{22} + \frac{U_{33}}{Sin^2\beta} + \frac{2U_{13}Cos\beta}{Sin^2\beta}\right]$$



1 Hetisine

EXPERIMENTAL

The crystals of hetisine perchlorate were prepared by slow evaporation after dissolving hetisine in perchloric acid. *Crystal data:* Molecular formula $(C_{20}H_{28}HO_3)\oplus(ClO_4)\ominus$, MW=429.90, space group $P2_1$, a=11.078(2)Å, b=9.463(1)Å, c=18.801(2)Å, β=93.20(2)°, Z=4, d_c=1.448 g/cm^3.

All measurements were carried out using a CAD-4 diffractometer. The unit cell parameters were refined using 25 reflections from different regions of the reciprocal space with 2θ between 60 and 70°. The intensity data were measured by an ω/θ scan using Ni filtered CuKα (λ=1.5418 Å); 2θ<150°; Δω=0.70+0.14 tan (θ)° for the peak and 25% on each side for background; aperture 3+0.4 tan θ (mm). A total of 4320 unique reflections were measured of which 4004 had $|Fo| \geq 1.4\ \sigma(F)$ and were used for the least squares and structure determination.

The structure was solved by multisolution methods (7) using the program MULTAN 80 (8) and refined using block-diagonal least squares to an R of 0.069 for 4004 observed reflections. All the 58 nonhydrogen atoms were refined anisotropically. A total of 49 hydrogens were located by stereochemical considerations and from a difference electron density map. They were refined isotropically. The quantity minimized in the refinement was $w|\Delta F|^2$, where $w = 1/\sigma(F)^2$ and where σ (F) is the standard deviation in the observed structure factors estimated from counting statistics. During the refinement, we noticed that the oxygens of one of the perchlorate ions have high temperature factors, indicating a disorder. The final electron density map had a residual peak of about one-sixth the strength of a carbon atom at x=0.75, y=0.19, and z=0.17. Otherwise, the electron density map was featureless. The scattering factors were taken from the *International Tables for X-ray Crystallography* (9). The coordinates and thermal parameters of the nonhydrogen atoms are given in Table 3. A list of structure factors, anisotropic thermal parameters of nonhydrogen atoms, and positional and thermal parameters of hydrogen are available from the senior author.

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