

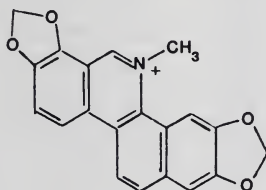
The Crystal and Molecular Structure of Oxysanguinarine Obtained from *Sanguinaria canadensis* L., Papaveraceae¹

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Introduction

Bloodroot² is a common wildflower which blooms in early spring throughout Indiana and neighboring states. Its name is derived from the bright red excretion obtained when the tubular root is broken. The plant was used as a source of red dye by American Indians, and its extracts have been investigated for medicinal uses as well.

The principal component of the dye, sanguinarine (1) has been characterized by degradation chemistry (3), although no definitive studies by X-ray crystallography have been reported. This project was undertaken to confirm the identity of the dye and to accurately determine its three dimensional structure.



(1)

Experimental

Approximately 400 grams of fresh root were collected and used in the separation process. Aqueous extraction followed by alumina column chromatography yielded a yellow fraction from which small red-orange crystals were obtained by repeated crystallizations. A suitable crystal was affixed to a glass fiber and transferred to the diffractometer for characterization. The diffractometer used was a Picker goniostat controlled by a locally designed automation package and has been described in detail elsewhere (1).

A systematic search of a limited hemisphere of reciprocal space located a set of diffraction maxima with no systematic extinctions or symmetry. Statistical tests indicated the centrosymmetric space group $P\bar{1}$, and subsequent solution and refinement of the structure confirmed this choice. All data were collected at -161°C . Cell data, based on a least squares fit of angular data from 30 carefully centered reflections, are $a = 8.221(2)$, $b = 11.950(4)$, $c = 7.981(2)\text{ \AA}$, $\alpha = 101.28(1)$, $\beta = 107.09(2)$, $\gamma = 81.85(2)^{\circ}$. A calculated density of 1.576 g/cm^3 for $Z = 2$ is reasonable for compounds of this type. A total of 1919 unique data were collected, of which 1615 were considered observed³ and used in the solution and refinement.

The structure was solved by a combination of direct methods and Fourier techniques⁴, and refined by full-matrix least squares. Hydrogen atoms were refined isotropically, with all non-hydrogen atoms assigned anisotropic thermal parameters. Final residuals are $R(F) = 0.047$ and $R_w(F) = 0.049$. A final difference Fourier was featureless, with the largest peak being 0.3 e/\AA^3 . Final fractional coordinates and thermal parameters are given in Table 1, with the atom numbering scheme shown in the ORTEP drawing of Figure 1. Complete crystallographic details are available⁵.

TABLE I. Fractional Coordinates for Oxysanguinarine

Atom	x*	y	z	10B _{iso}
C(1)	3014(4)	4219(3)	14(4)	24
C(2)	2034(4)	4944(2)	-1065(4)	25
C(3)	431(4)	4712(3)	-2204(4)	25
C(4)	-225(4)	3717(3)	-2374(4)	26
C(5)	255(4)	1784(3)	-1569(4)	24
C(6)	1258(4)	962(3)	-691(4)	24
N(7)	4643(3)	2632(2)	2556(3)	21
C(8)	5847(4)	1831(2)	3372(4)	22
C(9)	6526(4)	-212(3)	3710(4)	22
C(10)	6095(4)	-1318(3)	3390(4)	25
C(11)	4615(4)	-1644(3)	2164(4)	27
C(12)	3542(4)	-823(3)	1270(4)	26
C(13)	2804(4)	1205(2)	657(4)	21
C(14)	3252(4)	2327(2)	1079(4)	20
C(15)	2354(4)	3167(2)	-27(4)	21
C(16)	766(4)	2900(3)	-1295(4)	22
C(17)	3910(4)	315(2)	1595(4)	21
C(18)	5462(4)	637(2)	2860(4)	21
O(19)	8069(3)	-109(2)	4969(3)	29
C(20)	8639(4)	-1234(3)	5433(5)	28
O(21)	7336(3)	-1978(2)	4445(3)	32
O(22)	-252(3)	5613(2)	-3121(3)	30
C(23)	922(4)	6466(3)	-2449(5)	31
O(24)	2435(3)	5987(2)	-1259(3)	32
C(25)	4686(5)	3784(3)	3626(5)	28
O(26)	7112(3)	2155(2)	4563(3)	27
H(27)	409(4)	441(3)	79(4)	32(7)
H(28)	-121(4)	353(3)	-314(4)	32(8)
H(29)	-79(4)	160(2)	-244(4)	15(6)
H(30)	98(3)	19(2)	-93(4)	14(6)
H(31)	249(3)	-107(2)	35(3)	2(5)
H(32)	436(4)	-235(3)	203(4)	20(6)
H(33)	974(4)	-145(2)	512(4)	18(6)
H(34)	874(4)	-118(3)	672(5)	33(7)
H(35)	121(5)	671(3)	-352(5)	56(9)
H(36)	51(4)	713(3)	-171(4)	33(8)
H(37)	555(4)	422(3)	340(4)	28(7)
H(38)	492(4)	371(2)	493(4)	26(7)
H(39)	355(4)	420(3)	334(4)	31(7)

*Fractional coordinates are $\times 10^4$ for non-hydrogen atoms and $\times 10^3$ for hydrogen atoms.

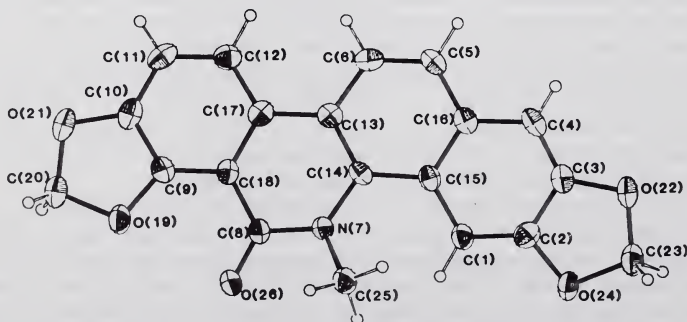


FIGURE 1: ORTEP drawing of molecule showing numbering scheme. All atoms are drawn at 50% probability, except for hydrogens which are assigned arbitrary fixed values.

Results and Discussion

As seen in the figure, the single crystal selected was shown by X-ray analysis to the oxysanguinarine. No attempt was made to determine if the oxysanguinarine is the component present in the root, or whether the separation techniques resulted in the oxidation of sanguinarine. Both the oxidized and reduced forms of the molecule have been reported to be the natural material (2). Principal bonded distances and angles for the molecule are given in Tables 2 and 3. The hydrogen atoms positions are well-

TABLE 2. Bonded Distances In Angstroms.

O(19)	C(9)	1.372(4)	C(3)	C(4)	1.340(5)
O(19)	C(20)	1.442(4)	C(4)	C(16)	1.431(4)
O(21)	C(10)	1.379(4)	C(5)	C(6)	1.356(4)
O(21)	C(20)	1.436(4)	C(5)	C(16)	1.413(4)
O(22)	C(3)	1.380(4)	C(6)	C(13)	1.427(4)
O(22)	C(23)	1.423(4)	C(8)	C(18)	1.460(4)
O(24)	C(2)	1.381(4)	C(9)	C(10)	1.373(4)
O(24)	C(23)	1.445(4)	C(9)	C(18)	1.386(4)
O(26)	C(8)	1.235(4)	C(10)	C(11)	1.366(5)
N(7)	C(8)	1.384(4)	C(11)	C(12)	1.383(5)
N(7)	C(14)	1.410(4)	C(12)	C(17)	1.394(4)
N(7)	C(25)	1.471(4)	C(13)	C(14)	1.391(4)
C(1)	C(2)	1.351(4)	C(13)	C(17)	1.467(4)
C(1)	C(15)	1.429(4)	C(14)	C(15)	1.446(4)
C(2)	C(3)	1.394(4)	C(15)	C(16)	1.429(4)
			C(17)	C(18)	1.425(4)

TABLE 3. Bonded Angles in Degrees.

C(9)	O(19)	C(20)	106.03(24)
C(10)	O(21)	C(20)	105.73(23)
C(3)	O(22)	C(23)	106.58(24)
C(2)	O(24)	C(23)	105.82(25)
C(8)	N(7)	C(14)	122.81(24)
C(8)	N(7)	C(25)	113.43(24)
C(14)	N(7)	C(25)	121.93(25)
C(2)	C(1)	C(15)	117.8(3)
O(24)	C(2)	C(1)	127.3(3)
O(24)	C(2)	C(3)	109.52(26)
C(1)	C(2)	C(3)	123.2(3)
O(22)	C(3)	C(2)	109.56(27)
O(22)	C(3)	C(4)	128.4(3)
C(2)	C(3)	C(4)	122.0(3)
C(3)	C(4)	C(16)	117.5(3)
C(6)	C(5)	C(16)	121.3(3)
C(5)	C(6)	C(13)	121.7(3)
O(26)	C(8)	N(7)	119.66(26)
O(26)	C(8)	C(18)	123.19(26)
N(7)	C(8)	C(18)	116.94(26)
O(19)	C(9)	C(10)	110.14(26)
O(19)	C(9)	C(18)	127.94(27)
C(10)	C(9)	C(18)	121.9(3)
O(21)	C(10)	C(9)	110.3(3)
O(21)	C(10)	C(11)	128.3(3)
C(9)	C(10)	C(11)	121.3(3)
C(10)	C(11)	C(12)	118.4(3)
C(11)	C(12)	C(17)	122.0(3)
C(6)	C(13)	C(14)	118.04(28)
C(6)	C(13)	C(17)	122.02(27)

TABLE 3—Continued.

C(14)	C(13)	C(17)	119.94(27)
N(7)	C(14)	C(13)	119.67(26)
N(7)	C(14)	C(15)	119.64(26)
C(13)	C(14)	C(15)	120.62(27)
C(1)	C(15)	C(14)	123.48(27)
C(1)	C(15)	C(16)	118.48(27)
C(14)	C(15)	C(16)	117.97(27)
C(4)	C(16)	C(5)	120.2(3)
C(4)	C(16)	C(15)	120.8(3)
C(5)	C(16)	C(15)	118.86(27)
C(12)	C(17)	C(13)	123.49(28)
C(12)	C(17)	C(18)	118.90(28)
C(13)	C(17)	C(18)	117.58(26)
C(8)	C(18)	C(9)	120.96(27)
C(8)	C(18)	C(17)	121.32(26)
C(9)	C(18)	C(17)	117.45(27)
O(19)	C(20)	O(21)	107.72(25)
O(22)	C(23)	O(24)	107.86(25)

determined, with the average C-H distance being 0.94 Å. All bond distances and angles are within the ranges normally expected. The molecule is approximately planar, although the steric interaction of the C(25) methyl with O(26) and the hydrogen on C(1) results in a significant bending of the molecule. The space filling drawing of Figure 2 illustrates this interaction.

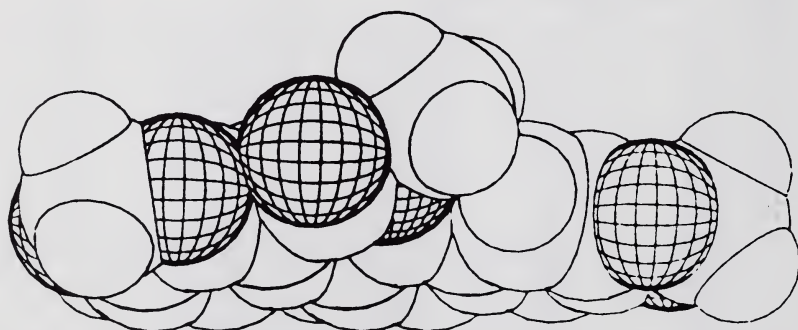


FIGURE 2: A space filling representation of oxysanguinarine showing the steric interaction of C(25) with the neighboring atoms.

Footnotes

1. This material is based upon work supported in part by National Science Foundation under Grant No. CHE-77-09496.
2. Other common names for sanguinaria are red puccoon, red root, puccoon root and tetterwort.
3. The data were considered observed if they met the criteria $I \geq 2.0 \times \sigma(I)$, where $\sigma(I)$ is the estimated error of the intensity based on counting statistics.
4. Programs used in this study included Main and Woolfson's MULTAN78, Johnson's

ORTEP, Smith's SPACFIL, various code adapted from the A. C. Larson Los Alamos series as well as locally developed programs.

5. Complete crystallographic details are available in microfiche form from the Chemistry Library, Indiana University, Bloomington, Indiana 47405. Request MSC Report #84200.

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