

Tetrachyrin

BY VOLKER ZABEL AND WILLIAM H. WATSON*

FASTBIOS Laboratory, Department of Chemistry, Texas Christian University, Fort Worth, Texas 76129, USA

AND NOBUO OHNO AND TOM J. MABRY

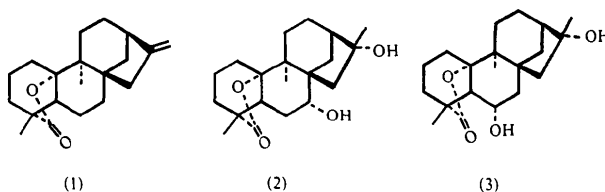
The Department of Botany, The University of Texas at Austin, Austin, Texas 78712, USA

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Abstract. $C_{20}H_{28}O_2$, $M_r = 300.23$, monoclinic, $P2_1$, $a = 10.783$ (3), $b = 11.151$ (2), $c = 7.016$ (2) Å, $\beta = 102.72$ (3)°, $V = 822.9$ (4) Å³, $Z = 2$, $d_c = 1.212$ Mg m⁻³. Full-matrix least-squares refinement (non-hydrogen atoms anisotropic, H atoms isotropic) based on 1484 reflexions led to a final R of 0.049. Tetrachyrin is a new type of rearranged kaurenoid diterpene lactone with the C(20) methyl group normally attached at C(10) shifted to the C(9) position. The A ring exhibits a slightly twisted chair conformation and is *trans*-fused to the B ring. The B ring is in a twist-boat conformation and is *trans*-fused to the C ring. The C ring exhibits a slightly distorted chair conformation with a five-membered ring formed by connection of the 1,3-diaxial substituents. The five-membered ring exhibits a folded envelope conformation with C(14) the flap. The five-membered lactone ring exhibits an envelope conformation with C(5) the flap.

Introduction. *Tetrachyrin orizabaensis* Sch. Bip, ex Klatt var. *websteri* Wussow & Uratsch (formerly *Calea orizabaensis* var. *websteri*) was investigated as part of a broad biochemical systematic survey of the tribe Heliantheae (family Compositae). Chromatographic separation of leaf and stem extracts yielded (–)-kaur-16-en-19-oic acid and a new diterpene named tetrachyrin (1) (Ohno, Mabry, Zabel & Watson, 1979). Tetrachyrin represents a new structural type of rearranged kaurenoid lactone where the methyl at C(10) has migrated to C(9). Two similar rearranged kaurenoids, eupatalbin (2), and eupatoralbin (3), were isolated recently from *Eupatorium album* L. (Herz, Govindan & Blount, 1979). *E. album* is a member of the Compositae family but belongs to the tribe Eupatorieae. The structures of tetrachyrin and eupatalbin were established by X-ray diffraction studies, and the absolute configurations of eupatalbin and eupatoralbin were inferred from a CD investigation

(Herz, Govindan & Blount, 1979). We now report in detail on the structure of tetrachyrin (1).



A crystal of dimensions 0.4 × 0.4 × 0.5 mm was used to collect intensity data on a Syntex $P2_1$ diffractometer system by the $\theta:2\theta$ scanning technique using a variable scan speed, a graphite monochromator and Cu $K\alpha$ radiation ($\lambda = 1.54178$ Å). Room-temperature lattice parameters were refined by a least-squares procedure utilizing 15 reflexions whose angles were measured by a centering routine associated with the Syntex diffractometer. Systematic absences were consistent with space group $P2_1$. A periodically monitored reflexion showed no significant change in intensity. Of the 1508 independent reflexions measured, 26 had intensities less than $2\sigma(I)$ and were not used in the refinement. One additional reflexion showed significant secondary extinction and was dropped from the final refinement. Lorentz and polarization corrections were applied, but no absorption corrections were made.

The direct-methods program *MULTAN* (Germain, Main & Woolfson, 1971) was used to calculate phases for the 300 $|E|$ values greater than 1.28. The phase set with the largest combined figure of merit was selected, and the E map calculated with these phases revealed the positions of all nonhydrogen atoms. Alternate least-squares refinements and difference Fourier calculations yielded the coordinates of all H atoms. Full-matrix least-squares refinement with H atoms included converged to an R of 0.049 where $R = \sum ||F_o| - |F_c|| / \sum |F_o|$. The function minimized in the refinement was $\sum w(|F_o| - |F_c|)^2$, where $w = 1/\sigma(I)$ was determined from counting statistics. H atom thermal parameters were refined isotropically.

* To whom correspondence should be addressed.

Table 1. Atomic positional parameters ($\times 10^4$, for H $\times 10^3$) for tetrachyrin

	x	y	z	$U_{eq}/U(\text{\AA}^2)^*$
C(1)	4161 (3)	3388 (3)	3373 (3)	6.3
C(2)	5586 (3)	3576 (4)	3527 (4)	7.3
C(3)	6403 (3)	2787 (4)	5087 (5)	7.3
C(4)	5926 (2)	2777 (3)	6996 (4)	5.8
C(5)	4560 (2)	2274 (2)	6572 (3)	4.8
C(6)	4069 (3)	2000 (—)	8391 (3)	6.1
C(7)	2672 (3)	1687 (3)	7937 (3)	6.2
C(8)	1920 (2)	2128 (2)	5954 (3)	4.9
C(9)	2374 (2)	3390 (2)	5417 (4)	5.2
C(10)	3837 (2)	3326 (2)	5391 (3)	4.6
O(10)	4478 (2)	4379 (2)	6460 (3)	5.8
C(11)	1553 (3)	3771 (3)	3418 (5)	6.9
C(12)	121 (3)	3547 (4)	3157 (9)	8.3
C(13)	-115 (2)	2266 (3)	3744 (5)	6.4
C(14)	479 (2)	2128 (3)	5919 (4)	6.3
C(15)	1906 (2)	1221 (2)	4267 (3)	4.8
C(16)	650 (2)	1387 (3)	2846 (3)	5.6
C(17)	308 (4)	847 (4)	1126 (4)	7.6
C(18)	5660 (3)	4076 (3)	7430 (3)	6.0
O(18)	6347 (2)	4782 (3)	8431 (3)	8.0
C(19)	6866 (3)	2186 (4)	8654 (6)	8.4
C(20)	2184 (3)	4314 (3)	6977 (7)	8.2
H(1a)	364 (4)	265 (4)	272 (6)	7.8
H(1b)	366 (4)	402 (4)	230 (6)	7.5
H(2a)	576 (3)	430 (4)	367 (5)	6.5
H(2b)	556 (4)	348 (5)	211 (7)	8.8
H(3a)	731 (4)	314 (4)	539 (6)	8.2
H(3b)	643 (7)	204 (9)	466 (10)	14.7
H(5)	449 (5)	156 (6)	621 (7)	10.5
H(6a)	454 (4)	121 (4)	903 (5)	7.5
H(6b)	418 (3)	274 (4)	917 (5)	6.2
H(7a)	256 (4)	81 (4)	776 (5)	7.5
H(7b)	223 (4)	196 (4)	894 (5)	7.1
H(11a)	154 (5)	478 (6)	347 (7)	9.9
H(11b)	178 (3)	328 (4)	225 (5)	6.6
H(12a)	-27 (7)	407 (8)	378 (8)	11.4
H(12b)	-36 (6)	367 (6)	203 (7)	9.6
H(13)	-112 (3)	203 (4)	355 (4)	6.3
H(14a)	20 (3)	139 (3)	630 (4)	4.1
H(14b)	22 (3)	271 (3)	682 (4)	4.5
H(15a)	278 (5)	118 (7)	354 (7)	11.9
H(15b)	183 (3)	34 (3)	455 (4)	5.8
H(17a)	96 (5)	20 (5)	89 (6)	9.1
H(17b)	-33 (5)	89 (4)	34 (7)	8.2
H(19a)	648 (6)	205 (7)	982 (8)	11.7
H(19b)	769 (10)	272 (14)	869 (13)	16.2
H(19c)	724 (14)	136 (16)	858 (17)	18.9
H(20a)	252 (4)	516 (5)	686 (6)	7.9
H(20b)	275 (11)	413 (12)	819 (15)	16.5
H(20c)	119 (6)	438 (7)	677 (7)	10.8

$$* U_{eq} = (U_1 U_2 U_3)^{1/3}.$$

A final difference map showed no peak larger than $0.2 e \text{\AA}^{-3}$ and the largest shift during the final cycle of refinement was 0.3σ . Atomic scattering factors and the real and imaginary contributions to the anomalous dispersion were taken from *International Tables for X-ray Crystallography* (1974). Atomic positional parameters and U_{eq} values are given in Table 1 while

Table 2. Interatomic distances (\AA)

C(1)—C(2)	1.530 (4)	C(8)—C(15)	1.555 (3)
C(1)—C(10)	1.533 (3)	C(9)—C(10)	1.584 (3)
C(2)—C(3)	1.525 (5)	C(9)—C(11)	1.545 (4)
C(3)—C(4)	1.537 (5)	C(9)—C(20)	1.549 (5)
C(4)—C(5)	1.543 (3)	C(10)—O(10)	1.480 (3)
C(4)—C(18)	1.521 (4)	O(10)—C(18)	1.349 (3)
C(4)—C(19)	1.515 (5)	C(11)—C(12)	1.534 (5)
C(5)—C(6)	1.517 (3)	C(12)—C(13)	1.523 (5)
C(5)—C(10)	1.544 (3)	C(13)—C(14)	1.527 (4)
C(6)—C(7)	1.510 (4)	C(13)—C(16)	1.506 (4)
C(7)—C(8)	1.528 (3)	C(15)—C(16)	1.506 (3)
C(8)—C(9)	1.563 (3)	C(16)—C(17)	1.326 (4)
C(8)—C(14)	1.549 (3)	C(18)—O(18)	1.197 (4)

Table 3. Valence angles ($^\circ$)

C(2)C(1)C(10)	111.7 (2)	C(10)C(9)C(11)	112.0 (2)
C(1)C(2)C(3)	112.6 (3)	C(10)C(9)C(20)	109.0 (2)
C(2)C(3)C(4)	112.3 (3)	C(11)C(9)C(20)	108.7 (2)
C(3)C(4)C(5)	108.8 (2)	C(1)C(10)C(5)	109.8 (2)
C(3)C(4)C(18)	106.4 (2)	C(1)C(10)C(9)	116.0 (2)
C(3)C(4)C(19)	112.1 (3)	C(1)C(10)O(10)	104.9 (2)
C(5)C(4)C(18)	99.8 (2)	C(5)C(10)C(9)	114.5 (2)
C(5)C(4)C(19)	116.1 (3)	C(5)C(10)O(10)	101.9 (1)
C(18)C(4)C(19)	112.6 (3)	C(9)C(10)O(10)	108.2 (2)
C(4)C(5)C(6)	114.0 (2)	C(9)C(11)C(12)	115.1 (3)
C(4)C(5)C(10)	100.1 (2)	C(11)C(12)C(13)	110.2 (3)
C(6)C(5)C(10)	112.1 (2)	C(12)C(13)C(14)	107.8 (3)
C(5)C(6)C(7)	112.7 (2)	C(12)C(13)C(16)	110.9 (3)
C(6)C(7)C(8)	115.0 (2)	C(14)C(13)C(16)	101.8 (2)
C(7)C(8)C(9)	112.2 (2)	C(8)C(14)C(13)	102.4 (2)
C(7)C(8)C(14)	110.1 (2)	C(8)C(15)C(16)	106.3 (2)
C(7)C(8)C(15)	113.5 (2)	C(13)C(16)C(15)	107.4 (2)
C(9)C(8)C(14)	111.2 (2)	C(13)C(16)C(17)	127.4 (3)
C(9)C(8)C(15)	110.7 (2)	C(15)C(16)C(17)	125.2 (3)
C(14)C(8)C(15)	98.4 (2)	C(4)C(18)O(18)	109.7 (2)
C(8)C(9)C(10)	109.1 (2)	C(4)C(18)O(18)	128.6 (2)
C(8)C(9)C(11)	108.6 (2)	O(10)C(18)C(18)	121.7 (3)
C(8)C(9)C(20)	109.4 (2)	C(10)O(10)C(18)	109.9 (3)

interatomic distances and valence angles are presented in Tables 2 and 3.*

Discussion. Fig. 1 is an *ORTEP* drawing (Johnson, 1965) of tetrachyrin. Tetrachyrin (1) and the recently reported compounds eupatalbin (2) and eupatoralbin (3) (Herz, Govindan & Blount, 1979) represent a new structural type of rearranged kaurenoid lactone. The methyl group found normally at C(10) has migrated to the C(9) position and is replaced by a C(10) hydroxyl group. The C(10) hydroxyl then participates in the formation of a lactone ring through reaction with a C(18) acid function. The C(16)—C(17) double bond found in tetrachyrin is replaced by a C(16) hydroxyl group in eupatalbin. The change in hybridization at C(16) leads to changes in angles and distances within

* Lists of structure factors and thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35502 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

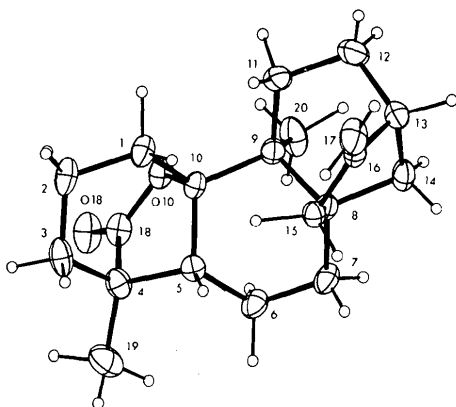


Fig. 1. ORTEP drawing of tetrachyrin. Thermal ellipsoids are drawn at the 35% probability level. H atoms are shown as spheres of arbitrary radius.

the five-membered ring which in turn are transmitted to the six-membered *C* ring (conformational transmission). All equivalent bonds in tetrachyrin and eupatalbin agree within 3σ except for C(6)–C(7), C(8)–C(14) and C(9)–C(11). Relative to the distances in tetrachyrin the C(8)–C(14) distance is contracted in eupatalbin to 1.535 (4) Å, while the C(9)–C(11) distance is expanded to 1.564 (4) Å. The C(6)–C(7) distance in eupatalbin of 1.530 (4) Å is longer because of the additional hydroxyl group at C(7). Several valence angles associated with the five-membered ring and the *C* ring differ significantly in the two compounds. This is brought about by the change in the C(13)C(16)C(15) angle from 107.4 (2) to 103.4 (4)° upon going from sp^2 to sp^3 hybridization.

Table 4 lists the torsion angles for tetrachyrin and eupatalbin. The *A* ring in both compounds exists as a slightly distorted chair conformation. The *A* ring is *trans*-fused to the *B* ring which exhibits a twist-boat conformation. The *C* ring is *trans*-fused to the *B* ring and is found in a slightly distorted chair conformation in both compounds. The five-membered ring is formed by connecting the 1,3-diaxial C atoms. In tetrachyrin the five-membered ring exhibits a folded envelope conformation with C(14) the flap. The five-membered ring in eupatalbin is in a folded half-chair conformation. The lactone ring in both compounds is in an envelope conformation with C(5) the flap. The absolute configuration shown in the ORTEP drawing is consistent with that inferred from CD data (Herz, Govindan & Blount, 1979).

Table 4. Torsion angles (°)

	Tetrachyrin	Eupatalbin*
Ring A		
1–2–3–4	–44.7 (4)	–45.0
2–3–4–5	60.8 (3)	61.6
3–4–5–10	–71.0 (3)	–71.4
4–5–10–1	71.1 (2)	70.3
5–10–1–2	–59.9 (3)	–58.2
10–1–2–3	43.9 (4)	43.4
Ring B		
5–6–7–8	–21.2 (3)	–24.9
6–7–8–9	–37.4 (3)	–34.0
7–8–9–10	58.5 (2)	55.7
8–9–10–5	–21.3 (2)	–18.3
9–10–5–6	–35.1 (2)	–37.7
10–5–6–7	58.7 (2)	62.1
Ring C		
8–9–11–12	44.4 (3)	43.8
9–11–12–13	–49.4 (5)	–45.5
11–12–13–14	63.5 (4)	58.7
12–13–14–8	–71.9 (3)	–70.0
13–14–8–9	69.1 (2)	73.1
14–8–9–11	–55.3 (3)	–59.2
Five-membered ring		
8–15–16–13	–5.6 (3)	11.5
15–16–13–14	–24.0 (3)	–37.8
16–13–14–8	44.8 (3)	51.2
13–14–8–15	–47.0 (2)	–43.1
14–8–15–16	32.1 (2)	18.9
Lactone ring		
4–5–10–O(10)	–39.7 (2)	–39.6
5–10–O(10)–18	24.0 (2)	24.9
10–O(10)–18–4	2.6 (3)	0.9
O(10)–18–4–5	–27.9 (3)	–26.3
18–4–5–10	40.2 (2)	39.5

* The average standard deviation is 0.4°.

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References

- GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* **A27**, 368–376.
 HERZ, W., GOVINDAN, W. V. & BLOUNT, J. F. (1979). *J. Org. Chem.* **44**, 2999–3003.
International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press.
 JOHNSON, C. K. (1965). ORTEP. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.
 OHNO, N., MABRY, T. J., ZABEL, V. & WATSON, W. H. (1979). *Phytochemistry*, **18**, 1687–1689.