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Anonamine, $C_{19}H_{27}NO_7$, Neosenkirkine, $C_{19}H_{27}NO_6$, and Hydroxysenkirkine, $C_{19}H_{27}NO_7.CH_3OH$. Macrocyclic Secopyrrolizidine Alkaloids from *Senecio anonymus* Wood

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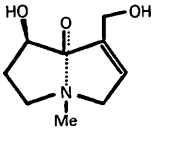
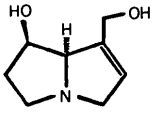
Abstract. λ(Mo $K\bar{\alpha}$) = 0·71069 Å, T = 298 K. Anonamine (I) (12,21-dihydroxy-4-methyl-4,8-secosenecionan-8,11,16-trione): $C_{19}H_{27}NO_7$, M_r = 381·2, monoclinic, $C2$, a = 24·247 (7), b = 8·766 (2), c = 9·072 (1) Å, β = 99·21 (2)°, U = 1903·3 (8) Å^3, Z = 4, D_m = 1·32 (1), D_x = 1·330 g cm^{-3}, μ(Mo $K\bar{\alpha}$) = 1·09 cm^{-1}, $F(000)$ = 816. Neosenkirkine (II) (12-hydroxy-4-methyl-4,8-secosenecionan-8,11,16-trione): $C_{19}H_{27}NO_6$, M_r = 365·2, monoclinic, $C2$, a = 24·45 (1), b = 8·781 (2), c = 9·029 (2) Å, β = 98·99 (3)°, U = 1915 (1) Å^3, Z = 4, D_m = 1·27 (1), D_x = 1·267 g cm^{-3}, μ(Mo $K\bar{\alpha}$) = 1·01 cm^{-1}, $F(000)$ = 784. Hydroxysenkirkine (III) [12,18-dihydroxy-4-methyl-4,8-secosenecionan-8,11,16-trione–methanol (1/1)]: $C_{19}H_{27}NO_7.CH_3OH$, M_r = 413·2, orthorhombic, $P2_12_12_1$, a = 9·052 (3), b = 13·150 (4), c = 17·404 (8) Å, U = 2071 (1) Å^3, Z = 4, D_m = 1·33 (1), D_x = 1·325 g cm^{-3}, μ(Mo $K\bar{\alpha}$) = 1·10 cm^{-1}, $F(000)$ = 888. Full-matrix least squares refinement converged at R values of 0·042, 0·043 and 0·051 for 3163, 2894 and 2896 reflections for (I), (II) and (III), respectively. All three crystals exhibit hydrogen bonds, including intramolecular O11···HO12 and intermolecular O8···HO12. In addition, intermolecular hydrogen bonds appear in (I) between O21···HO21′ and in (III) between O8···HOCH$_3$. The observed N···C8 distances across the eight-membered otonecine rings were 2·200, 2·245 and 1·712 Å in (I), (II) and (III) respectively.

Introduction. Anonamine† (I), neosenkirkine (II) and hydroxysenkirkine (III) belong to a sub-group of pyrrolizidine alkaloids of the 12-membered macrocyclic diester type, which contain the seconecine otonecine (IV). At present, approximately two dozen members of this sub-group have been reported (Mattocks, 1986) and, of these, X-ray crystallographic studies have been reported for otosenine (Perez-Salazar, Cano, Fayos, Martínez-Carrera & García-Blanco, 1977), fukinotoxin (Furuya, Hikichi & Iitaka, 1976), senkirkine (Birnbaum, 1974) and clivorine (Birnbaum, 1972).

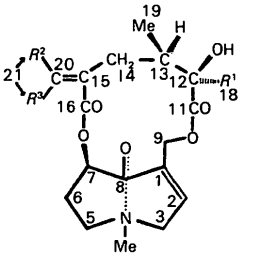
The 12-membered macrocyclic diesters of otonecine show the same pattern of hepatotoxicity observed for other pyrrolizidine alkaloids containing a double bond at C1–C2 (Mattocks, 1986; Peterson & Culvenor, 1983). In addition, it has recently been shown that four



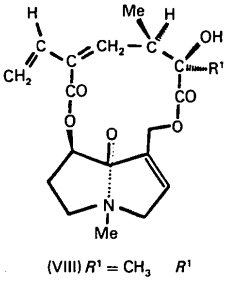
(IV)



(V)



(I) R^1 = CH_3, R^2 = CH_2OH, R^3 = H
(II) R_1 = CH_3, R^2 = CH_3, R^3 = H
(III) R^1 = CH_2OH, R^2 = H, R^3 = CH_3
(VI) R^1 = CH_3, R^2 = H, R^3 = CH_3
(VII) R^1 = CH_3, R^2 = H, R^3 = CH_3, epoxide (15*S*, 20*S*) in place of Δ^{15}.



(VIII) R^1 = CH_3 R^1

members of the group (clivorine, fukinotoxin, senkirkine and ligularidine) are mutagenic and one of these (fukinotoxin) is a known carcinogen (Yamanaka, Nagao & Sugimura, 1979). It has been pointed out that, in the past, the danger of pyrrolizidine alkaloids to human health has not been sufficiently recognized, especially in light of the worldwide presence of plants containing them (estimated at 3% of the world's flowering plants) (Smith & Culvenor, 1981). The three

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† This is the trivial name which has been given to this new alkaloid.

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Table 1. *X-ray data collection and solution*

	Anonamine (I)	Neosenkirkine (II)	Hydroxysenkirkine (III)
Crystal size (mm)	0·68 × 0·60 × 0·50	0·88 × 0·32 × 0·10	0·65 × 0·70 × 0·31
No. of reflections for lattice parameters	15	15	15
Diffractometer	Syntex $P2_1$	Syntex $P2_1$	Syntex $P2_1$
Radiation	Mo $K\bar{\alpha}$, $\lambda = 0.71069$ Å; graphite monochromator		
2θ range (°) for orientation matrix and lattice parameters	14·15–24·85	14·15–24·85	14·15–24·85
Scan type	ω	ω	ω
Scan speed (° min^{-1})	3·91–29·30	3·91–29·30	3·91–29·30
2θ range (data collection) (°)	4–50	4–40	4–50
h, k, l range	±28, ±10, 0–10	±28, ±10, 0–10	±10, 0–15, 0–20
No. of reflections measured	3510	3526	3164
No. of reflections with $F > 3\sigma(F)$	3163	2894	2896
R	0·042	0·043	0·051
wR	0·045	0·043	0·062
Weight = $k/[(\sigma F)^2 + gF^2]$ $k; g$	2·1; 0·0004	1·5; 0·0004	1·0; 0·3
Max. Δ/σ	0·041	0·041	0·027
Max., min. in $\Delta\rho$ (e Å^{-3})	0·51, −0·29	0·34, −0·24	0·36, −0·26

alkaloids described in this communication were isolated from a local weed, *Senecio anonymus* Wood, which was found to contain, in addition to these three, three other 12-membered macrocyclic diesters of otonecine (senkirkine, hydroxyneosenkirkine and otosenine) and four 12-membered macrocyclic diesters of retronecine (V) (senecionine, integerrimine, retrorsine and usaramine) (Zalkow, 1988). Anonamine (I) is a new pyrrolizidine alkaloid.

Experimental. Anonamine (I), neosenkirkine (II) and hydroxysenkirkine (III) were isolated from the ethanol extract of *Senecio anonymus* Wood using droplet counter-current chromatography (Zalkow, 1988). Crystals of (I) and (II) were obtained from acetonitrile, while crystals of (III) were obtained from methanol upon slow diffusion of acetone vapors. Specific optical rotations and melting points (corrected) were as follows: (I): $[\alpha]_D^{25°} + 33·5°$ (*c* 1, $CHCl_3$), m.p. 475 K; (II): $[\alpha]_D^{25°} + 16·9°$ (*c* 1, $CHCl_3$), m.p. 473–475 K; (III): $[\alpha]_D^{25°} -9·1°$ (*c* 1, C_2H_5OH), m.p. 393 K.

Experimental details for the X-ray examinations are given in Table 1. All densities determined by flotation in hexane–CCl_4. Lp corrections but no extinction or absorption corrections. Structures (I) and (III) solved in the same manner. *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978) used to generate a series of *E* maps, one of which correctly located most non-H atoms; after three cycles of full-matrix least-squares refinement (on *F*), remaining non-H atoms located from difference Fourier map; non-H atoms refined anisotropically and H atoms located from subsequent difference Fourier map. The structure of (II) was solved after observing the great similarity between the cell constants for (I) and (II), suggesting isomorphous structures. Thus, a solution was obtained by refining the coordinates of the non-hydrogen atoms [minus O(21) from (I)] with the observed data for (II). Parameters varied: overall scale factors, coordinates of non-H atoms, anisotropic temperature factors of non-H atoms, isotropic temperature factors for H atoms. Scattering factors as in *SHELX*76 (Sheldrick, 1976).

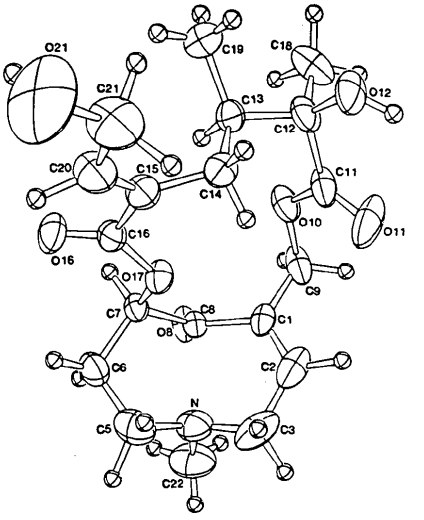

Fig. 1. *ORTEP*II view (Johnson, 1976) of anonamine (I) with the atom numbering. Thermal ellipsoids are drawn at the 50% probability level.

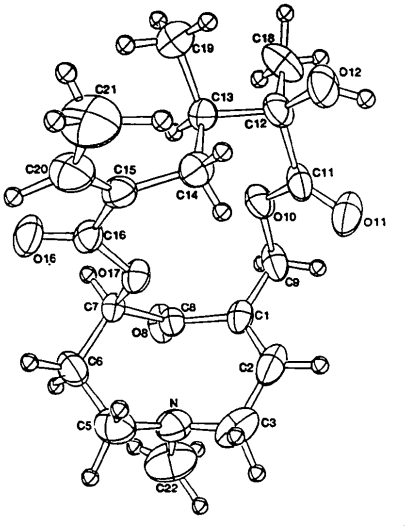

Fig. 2. *ORTEP*II view of neosenkirkine (II).

The absolute configurations of the three compounds are defined by reference to the known absolute configuration of otonecine as found in retusamine (Wunderlich, 1967).

Discussion. The *ORTEP*II (Johnson, 1976) views of anonamine (I), neosenkirkine (II) and hydroxysenkirkine (III) are shown in Figs. 1, 2 and 3, respectively, using 50% probability ellipsoids. The thermal parameters of the H atoms have been artificially reduced to clarify the pictures. The crystal packing of both (I) and (II), since they are isomorphous, is shown by the same figure (Fig. 4). Additional intermolecular hydrogen bonding between O21···HO21′ in (I) is shown in Fig. 5. Molecules of (III) exhibit intermolecular hydrogen bonds involving O8 and CH_3OH (see Fig. 6). Final atom coordinates, bond lengths and angles are given in Tables 2–6.* In Table 7 selected values used in describing structures of some secopyrrolizidine alkaloids are collected.

In all the known 12-membered macrocyclic esters of otonecine and retronecine with the C15–C20 exocyclic double bond, the esterifying chains assume very similar conformations (Mackay & Culvenor, 1982). The position of the C16–O16 carbonyl on the outer side of the pyrrolizidine skeleton remains virtually the same in all macrocyclic pyrrolizidine alkaloids, regardless of the size of the ester chain, and most likely is determined by steric hindrance of the inner (β) side of the pyrrolizidine skeleton. The less sterically restricted carbonyl, C11–O11, assumes a position roughly parallel to C16–O16 but pointing in the opposite

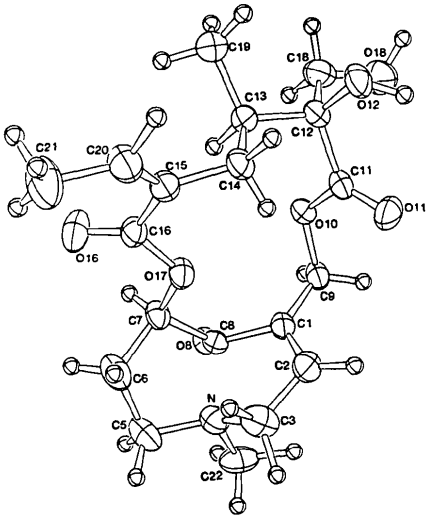

Fig. 3. *ORTEP*II view of hydroxysenkirkine (III).

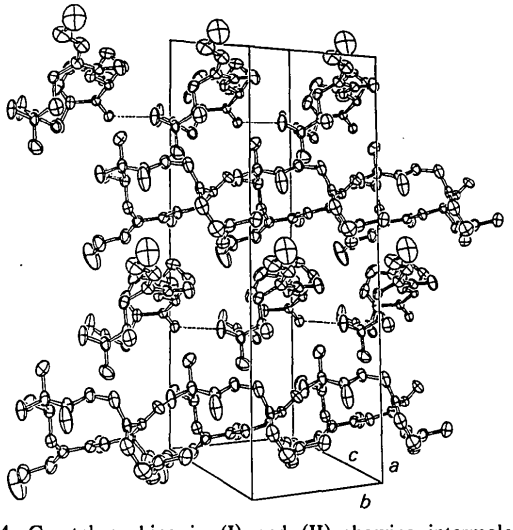

Fig. 4. Crystal packing in (I) and (II) showing intermolecular hydrogen bonds O8···HO12′.

* Lists of structure factors, H-atom coordinates and anisotropic thermal parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44939 (47 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

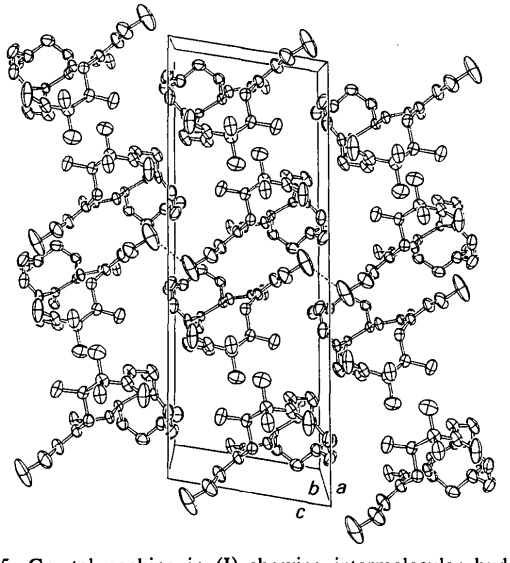

Fig. 5. Crystal packing in (I) showing intermolecular hydrogen bonds O21···HO21′.

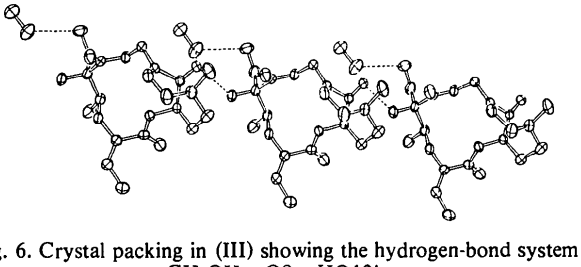

Fig. 6. Crystal packing in (III) showing the hydrogen-bond system CH_3OH···O8···HO12′.

direction. This orientation results from steric tension of the macrocyclic ring. Other influences are the intramolecular hydrogen bond O11···HO12, which contributes to the exceptional flatness of the fragment O11, C11, C12, O12, and a dipole–dipole repulsion of the two carbonyls. The two 1,3-unsaturated systems consisting of O8, C8, C1 and C2 and of O16, C16, C15 and C20 present in (I), (II) and (III) are subject to steric tension of the otonecine and macrocyclic rings, respectively, which results in non-planarity, found also in the structures of senkirkine (VI), otosenine (VII) and clivorine (VIII).

Table 2. *Final atomic coordinates and U_{eq} values* (Å²) *for anonamine* (I)

Here and in Tables 3 and 4 $U_{eq} = \frac{1}{3}\sum U_{ii}$.

	x	y	z	U_{eq}
C1	−0·82974 (9)	−0·2001	−0·0972 (2)	0·037
C2	−0·8625 (1)	−0·1558 (4)	−0·0039 (3)	0·060
C3	−0·9122 (1)	−0·2483 (5)	0·0160 (3)	0·078
C5	−0·9543 (1)	−0·4202 (4)	−0·1853 (3)	0·061
C6	−0·9285 (1)	−0·4629 (4)	−0·3178 (3)	0·050
C7	−0·88082 (8)	−0·3547 (3)	−0·3345 (2)	0·030
C8	−0·83967	−0·3451 (3)	−0·1850 (2)	0·029
C9	−0·7752 (1)	−0·1212 (3)	−0·1028 (3)	0·049
C11	−0·7963 (1)	0·1077 (4)	−0·2436 (3)	0·047
C12	−0·7940 (1)	0·1845 (3)	−0·3930 (3)	0·045
C13	−0·8332 (1)	0·0982 (3)	−0·5151 (2)	0·041
C14	−0·89317 (9)	0·0987 (3)	−0·4813 (2)	0·041
C15	−0·9294 (1)	−0·0200 (4)	−0·5675 (2)	0·042
C16	−0·91858 (8)	−0·1836 (3)	−0·5262 (2)	0·037
C18	−0·7336 (1)	0·1854 (4)	−0·4235 (4)	0·073
C19	−0·8309 (1)	0·1620 (4)	−0·6708 (3)	0·066
C20	−0·9706 (1)	0·0066 (4)	−0·6814 (3)	0·060
C21	−0·9905 (1)	0·1628 (5)	−0·7400 (4)	0·079
C22	−0·8896 (1)	−0·5199 (5)	0·0352 (4)	0·079
N	−0·90893 (9)	−0·3920 (3)	−0·0618 (2)	0·056
O8	−0·80485 (6)	−0·4475 (3)	−0·1629 (2)	0·041
O10	−0·77666 (7)	−0·0352 (3)	−0·2422 (2)	0·045
O11	−0·8122 (1)	0·1671 (3)	−0·1404 (2)	0·092
O12	−0·81442 (9)	0·3351 (3)	−0·3908 (2)	0·059
O16	−0·92665 (8)	−0·2893 (3)	−0·6123 (2)	0·054
O17	−0·89890 (6)	−0·2019 (3)	−0·3795 (1)	0·037
O21	−1·0288 (2)	0·1493 (5)	−0·8720 (4)	0·147

Table 3. *Final atomic coordinates and U_{eq} values* (Å²) *for neosenkirkine* (II)

	x	y	z	U_{eq}
C1	−0·8295 (1)	−0·2001	−0·0966 (3)	0·038
C2	−0·8631 (1)	−0·1574 (4)	−0·0026 (3)	0·059
C3	−0·9117 (2)	−0·2497 (5)	0·0184 (4)	0·079
C5	−0·9539 (1)	−0·4176 (4)	−0·1868 (4)	0·065
C6	−0·9275 (1)	−0·4619 (4)	−0·3196 (3)	0·050
C7	−0·88036 (9)	−0·3545 (3)	−0·3350 (2)	0·032
C8	−0·83929 (9)	−0·3447 (4)	−0·1868 (3)	0·033
C9	−0·7758 (1)	−0·1213 (4)	−0·1026 (3)	0·048
C11	−0·7947 (1)	0·1089 (4)	−0·2415 (3)	0·044
C12	−0·7929 (1)	0·1850 (4)	−0·3936 (3)	0·044
C13	−0·8327 (1)	0·0988 (3)	−0·5150 (3)	0·040
C14	−0·8918 (1)	0·0983 (4)	−0·4774 (3)	0·043
C15	−0·9281 (1)	−0·0178 (4)	−0·5652 (3)	0·041
C16	−0·9185 (1)	−0·1807 (4)	−0·5257 (3)	0·038
C18	−0·7336 (1)	0·1833 (4)	−0·4250 (5)	0·069
C19	−0·8308 (1)	0·1653 (5)	−0·6715 (3)	0·064
C20	−0·9682 (1)	0·0108 (4)	−0·6805 (3)	0·058
C21	−0·9870 (1)	0·1653 (6)	−0·7409 (5)	0·083
C22	−0·8926 (2)	−0·5222 (6)	0·0336 (5)	0·097
N	−0·9095 (1)	−0·3930 (4)	−0·0604 (3)	0·057
O8	−0·80535 (7)	−0·4476 (3)	−0·1638 (2)	0·047
O10	−0·77741 (7)	−0·0360 (3)	−0·2423 (2)	0·045
O11	−0·8090 (1)	0·1715 (3)	−0·1368 (2)	0·064
O12	−0·81237 (9)	0·3354 (3)	−0·3910 (2)	0·060
O16	−0·92716 (9)	−0·2860 (3)	−0·6121 (2)	0·056
O17	−0·89816 (7)	−0·2016 (3)	−0·3786 (2)	0·037

One of the most intriguing features of the seco-pyrrolizidine alkaloids is the short trans-annular distance of N···C8, being well below the sum of the van der Waals radii of 2·9 Å. This correlates with an unusually long C8—O8 carbonyl bond. Perez-Salazar *et al.* (1977) found it useful to interpret the results on otosenine (VII) with the electron-repulsion distribution theory (Linnett, 1966). The extent of the partial bond in senkirkine (VI) and clivorine (VIII) has been discussed

Table 4. *Final atomic coordinates and U_{eq} values* (Å²) *for hydroxysenkirkine* (III)

	x	y	z	U_{eq}
C1	0·8408 (2)	0·1694 (2)	0·8916 (1)	0·030
C2	0·8093 (2)	0·0732 (2)	0·8875 (2)	0·0390
C3	0·9232 (3)	0·0115 (2)	0·8450 (2)	0·049
C5	1·1598 (3)	0·0766 (3)	0·7842 (2)	0·052
C6	1·0869 (3)	0·1421 (2)	0·7245 (2)	0·048
C7	0·9869 (2)	0·2183 (2)	0·7651 (1)	0·031
C8	0·9885 (2)	0·1979 (2)	0·8535 (1)	0·029
C9	0·7564 (2)	0·2468 (2)	0·9364 (1)	0·033
C11	0·5271 (2)	0·2776 (2)	0·8716 (1)	0·031
C12	0·4499 (2)	0·3485 (2)	0·8148 (1)	0·033
C13	0·5370 (2)	0·3479 (2)	0·7383 (1)	0·034
C14	0·5440 (3)	0·2403 (2)	0·7047 (1)	0·036
C15	0·6563 (3)	0·2315 (2)	0·6415 (1)	0·033
C16	0·8127 (3)	0·2455 (2)	0·6645 (1)	0·032
C18	0·4420 (3)	0·4551 (2)	0·8508 (2)	0·046
C19	0·4727 (3)	0·4209 (2)	0·6791 (2)	0·053
C20	0·6205 (3)	0·2128 (3)	0·5683 (2)	0·047
C21	0·7182 (4)	0·2023 (4)	0·4999 (2)	0·068
C22	1·1387 (3)	0·0556 (2)	0·9238 (2)	0·052
N	1·0577 (2)	0·0767 (2)	0·8513 (1)	0·038
O8	1·0766 (2)	0·2575 (1)	0·8913 (1)	0·032
O10	0·6651 (2)	0·3108 (1)	0·88645 (9)	0·032
O11	0·4744 (2)	0·2014 (1)	0·8978 (1)	0·046
O12	0·3066 (2)	0·3126 (1)	0·7980 (1)	0·043
O16	0·9093 (2)	0·2839 (2)	0·6265 (1)	0·052
O17	0·8369 (2)	0·2094 (1)	0·73610 (9)	0·035
O18	0·3786 (2)	0·4513 (2)	0·9249 (1)	0·058
O	0·0714 (2)	0·4588 (2)	0·9020 (1)	0·058
C	−0·0333 (4)	0·4956 (3)	0·9543 (2)	0·057

Table 5. *Bond lengths* (Å) *with their e.s.d.'s in parentheses*

	(I)	(II)	(III)
C1–C2	1·309 (3)	1·324 (4)	1·298 (4)
C1–C8	1·498 (3)	1·508 (3)	1·539 (3)
C1–C9	1·500 (4)	1·493 (4)	1·492 (3)
C2–C3	1·486 (5)	1·476 (5)	1·506 (4)
C3–N	1·453 (4)	1·451 (5)	1·493 (3)
C5–C6	1·490 (4)	1·499 (4)	1·504 (4)
C5–N	1·461 (3)	1·463 (4)	1·489 (4)
C6–C7	1·522 (3)	1·512 (4)	1·523 (4)
C7–C8	1·522 (3)	1·545 (3)	1·562 (3)
C7–O17	1·448 (2)	1·447 (3)	1·454 (3)
C8–O8	1·227 (2)	1·222 (3)	1·298 (3)
C9–O10	1·468 (3)	1·462 (3)	1·466 (3)
C11–C12	1·522 (3)	1·534 (4)	1·528 (3)
C11–O10	1·339 (3)	1·341 (3)	1·348 (3)
C11–O11	1·188 (3)	1·192 (4)	1·200 (3)
C12–C13	1·537 (3)	1·546 (4)	1·547 (3)
C12–C18	1·533 (4)	1·520 (4)	1·537 (4)
C12–O12	1·410 (3)	1·406 (3)	1·412 (3)
C13–C14	1·533 (3)	1·535 (4)	1·532 (4)
C13–C19	1·529 (3)	1·537 (4)	1·525 (4)
C14–C15	1·498 (3)	1·495 (4)	1·503 (3)
C15–C16	1·494 (3)	1·485 (4)	1·483 (4)
C15–C20	1·339 (3)	1·338 (4)	1·336 (4)
C16–O17	1·350 (2)	1·356 (3)	1·351 (3)
C16–O16	1·207 (3)	1·207 (3)	1·208 (3)
C18–O18	—	—	1·413 (4)
C20–C21	1·520 (4)	1·507 (5)	1·490 (4)
C21–O21	1·398 (4)	—	—
C22–N	1·456 (4)	1·438 (5)	1·486 (4)

by Birnbaum (1974), who correlated the bond distances with the frequencies of the carbonyl peak in the infrared spectrum.

Table 6. *Angles* (°) *with e.s.d.'s in parentheses*

	(I)	(II)	(III)
C8–C1–C2	122·2 (2)	121·6 (2)	113·8 (2)
C9–C1–C2	121·0 (2)	122·0 (2)	125·5 (2)
C9–C1–C8	116·2 (2)	115·9 (2)	120·3 (2)
C3–C2–C1	120·3 (3)	121·3 (3)	113·7 (3)
N–C3–C2	107·8 (2)	108·7 (3)	102·3 (2)
N–C5–C6	107·4 (2)	107·6 (2)	105·6 (2)
C7–C6–C5	110·4 (2)	109·9 (2)	108·5 (2)
C8–C7–C6	109·9 (2)	110·9 (2)	109·8 (2)
O17–C7–C6	113·8 (2)	113·7 (2)	110·0 (2)
O17–C7–C8	108·6 (1)	108·1 (2)	109·7 (2)
C7–C8–C1	122·5 (2)	122·8 (2)	117·3 (2)
O8–C8–C1	119·1 (2)	119·0 (2)	117·5 (2)
O8–C8–C7	115·6 (2)	116·0 (2)	113·7 (2)
O10–C9–C1	111·5 (2)	111·4 (2)	111·7 (2)
O10–C11–C12	111·1 (2)	110·8 (2)	110·5 (2)
O11–C11–C12	124·7 (2)	124·2 (2)	125·0 (2)
O11–C11–O10	124·2 (2)	124·9 (3)	124·4 (2)
C13–C12–C11	108·5 (2)	108·5 (2)	108·7 (2)
C18–C12–C11	109·5 (2)	109·0 (2)	108·3 (2)
C18–C12–C13	111·7 (2)	112·1 (2)	112·3 (2)
O12–C12–C11	109·8 (2)	109·7 (2)	110·5 (2)
O12–C12–C13	107·1 (2)	107·1 (2)	106·8 (2)
O12–C12–C18	110·2 (2)	110·4 (2)	110·3 (2)
C14–C13–C12	110·5 (2)	110·8 (2)	110·8 (2)
C19–C13–C12	112·1 (2)	111·0 (2)	112·5 (2)
C19–C13–C14	111·1 (2)	111·7 (2)	109·8 (2)
C15–C14–C13	112·9 (2)	112·7 (2)	112·3 (2)
C16–C15–C14	118·1 (2)	118·1 (2)	115·9 (2)
C20–C15–C14	112·9 (2)	125·9 (2)	123·2 (2)
C20–C15–C16	116·1 (2)	115·9 (2)	120·8 (2)
O17–C16–C15	112·4 (2)	112·7 (2)	111·1 (2)
O16–C16–C15	124·8 (2)	125·3 (2)	126·5 (3)
O16–C16–O17	122·8 (2)	122·1 (2)	122·4 (2)
O18–C18–C12	—	—	111·0 (2)
C21–C20–C15	125·7 (3)	126·5 (3)	129·4 (2)
O21–C21–C20	110·7 (3)	—	—
C5–N–C3	115·3 (2)	115·5 (3)	116·6 (2)
C22–N–C3	114·3 (2)	115·1 (3)	110·9 (2)
C22–N–C5	117·7 (3)	117·0 (3)	111·0 (2)
C11–O10–C9	116·6 (2)	116·6 (2)	116·8 (2)
C16–O17–C7	115·6 (2)	116·1 (2)	116·3 (2)

Analysis of molecular packing in the crystals of (I), (II), (III), (VI), (VII) and (VIII) led us to the conclusion that both the distance of C8···N and the carbonyl C8–O8 bond length are dependent on the presence of hydrogen bonds involving O8. While the molecules of macrocyclic retronecine esters are intermolecularly hydrogen bonded through the nitrogen, all known X-ray structures of the secopyrrolizidines show hydrogen bonds involving O8. Thus, in the crystals of (I), (II), (III), (VI) and (VII) there are intermolecular hydrogen bonds O8···HO12′. The HO12 hydroxyl is also involved in an intramolecular hydrogen bond O11···HO12 [with the exception of (VII), in which the distance O11···HO12 exceeds the sum of the van der Waals O···H(O) radii of 2·6 Å]. This results in an exceptional flatness of the fragment O11–C11–C12–O12. Clivorine (VIII), which has no hydroxyl groups, crystallizes with a molecule of water binding molecules of the alkaloid through the links O8···H–O–H···O16 (Birnbaum, 1972). In hydroxysenkirkine the distance of C8···N is by far the shortest recorded in the series of free secopyrrolizidine alkaloids. Analysis of hydrogen bonds with O8 reveals the presence of two compared with only one in the remaining five alkaloids (Fig. 6). Besides the hydrogen bond O8···HO12′ already mentioned there is a second with a molecule of methanol present in the crystal, O8···HOCH$_3$ (distance OH···O8 is 1·548 and O···O8 is 2·653 Å). The hydroxyl from the methanol forms a second hydrogen bond with O18 (OH···O18 1·841 and O···O18 2·81 Å).

The hydrogen bonds to O8 decrease the sp^2 character of the carbonyl group and could reasonably

Table 7. *Comparison of selected values for some* 12*-membered macrocyclic otonecine esters*

	(I)	(II)	(III)	(VI)	(VII)	(VIII)
Intramolecular distances (Å)						
C8···N	2·200	2·245	1·712	2·292[1]	2·18[2]	1·993[3]
C8···O8	1·227	1·222	1·298	1·213[1]	1·26[2]	1·258[3]
O11···O12	2·700	2·700	2·731	2·680[1]	2·70*	—
O11···HO12	2·338	2·462	2·397	2·221[1]	3·19*	—
C16···C11	4·411	4·448	4·456	4·403*	4·31*	3·867*
O17···O10	3·359	3·350	3·322	3·348*	3·32*	3·130*
Intermolecular distances (Å)						
O12···O8	2·794	2·700	2·731	2·805[1]	2·84[2]	—
HO12···O8	1·974	1·989	1·939	2·14[1]	2·453*	—
Angle (°) between vectors of (C11, O11) and (C16, O16)	143·7	145·3	147·7	151·7	166·6*	145·6*
Torsion angles (°)						
O8–C8–C1–C2	116·2	115·4	134·1	113·7*	112·2*	114·8*
O16–C16–C15–C20	29·7	28·4	33·7	38·6*	38·4*	—
O11–C11–C12–O12	1·0	2·1	2·4	1·3*	7·8*	*139·9*
Angle (°) N–C8–O8	109·97	109·07	110·41	109·3[4]	—	110·2[4]
Displacement (Δ) (Å)	0·139	0·122	0·289	0·115[4]	—	0·213[4]

[1] Birnbaum (1974).
[2] Perez-Salazar *et al.* (1977).
[3] Birnbaum (1972).
[4] Dunitz (1979).
* Calculated from cell constants and coordinates given in corresponding paper.

account for the observed displacement (Δ) of C8 from the plane defined by the atoms to which it is bonded (Table 7). For compounds (I), (II) and (III), the observed out-of-plane displacements (Δ) are 0·139, 0·122 and 0·289 Å respectively. The more extensively O8 is hydrogen bonded, the more electron deficient C8 becomes and, thus, the more susceptible to interaction with the N lone pair. Therefore, the extent of hydrogen bonding to O8 can be correlated with the displacement (Δ) and in turn correlated with the C8—N bond length. This is consistent with the previous survey by Dunitz (1979) involving a number of compounds with interacting carbonyl and amino groups, where the C—N distances were correlated with the observed out-of-plane displacements.

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References

BIRNBAUM, G. I. (1974). *J. Am. Chem. Soc.* **96**, 6165–6168.
BIRNBAUM, K. B. (1972). *Acta Cryst.* B**28**, 2825–2833.
DUNITZ, J. A. (1979). *X-ray Analysis and the Structure of Organic Molecules*, pp. 367–370. New York: Cornell Univ. Press.
FURUYA, T., HIKICHI, M. & ITAKA, Y. (1976). *Chem. Pharm. Bull.* **24**, 1120–1122.
JOHNSON, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
LINNETT, J. W. (1966). *The Electronic Structures of Molecules. A New Approach*. London: Methuen.
MACKAY, M. F. & CULVENOR, C. C. J. (1982). *Acta Cryst.* B**38**, 2754–2758.
MAIN, P., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1978). *MULTAN*78. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.
MATTOCKS, A. R. (1986). *Chemistry and Toxicology of Pyrrolizidine Alkaloids*. London: Academic Press.
PEREZ-SALAZAR, A., CANO, F. H., FAYOS, J., MARTÍNEZ-CARRERA, S. & GARCÍA-BLANCO, S. (1977). *Acta Cryst.* B**33**, 3525–3527.
PETERSON, J. E. & CULVENOR, C. C. J. (1983). *Handbook of Natural Toxins*, edited by R. F. KEELER & A. T. TU, Chap. 19, pp. 637–671. New York: Decker.
SHELDRICK, G. M. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.
SMITH, L. W. & CULVENOR, C. C. J. (1981). *J. Nat. Products*, **44**, 129–152.
WUNDERLICH, J. A. (1967). *Acta Cryst.* **23**, 846–848.
YAMANAKA, H., NAGAO, M. & SUGIMURA, T. (1979). *Mutat. Res.* **68**, 211–216.
ZALKOW, L. H. (1988). In preparation.

Acta Cryst. (1988). C**44**, 1598–1600

Structure of Dibenzo[*a*,*g*]cyclotrideca-4a,8a-diene-5,7-diyn-15-one

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Abstract. $C_{21}H_{16}O$, $M_r = 284{\cdot}36$, monoclinic, $P2_1/c$, $a = 14{\cdot}442$ (3), $b = 17{\cdot}917$ (3), $c = 6{\cdot}085$ (1) Å, $\beta = 94{\cdot}17$ (1)°, $V = 1570{\cdot}4$ Å^3, $Z = 4$, $D_x = 1{\cdot}204$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, μ(Cu $K\alpha$) = 0·487 mm^{-1}, $F(000) = 600$, $T = 290$ (1) K, $R = 0{\cdot}078$ for 1039 observed reflections. In the structure reported here, the 13-membered ring contains seven synperiplanar, two antiperiplanar and four anticlinal conformational units. The diyne system is slightly nonlinear. The phenyl rings are not coplanar but are twisted with respect to each other by 27°.

Introduction. The title compound (1) was prepared (Acheson & Lee, 1987) by a synthetic route expected to

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