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Structure of Tetra-1-naphthoide*

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Abstract. $C_{44}H_{24}O_8$, $M_r = 680{\cdot}7$, tetragonal, $P4_2/n$ (second setting), $a = 13{\cdot}1416\ (16)$, $c = 9{\cdot}719\ (3)$ Å, $V = 1678{\cdot}5\ (4)$ Å^3, $Z = 2$, $D_x = 1{\cdot}347$ Mg m^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}71069$ Å, $\mu = 0{\cdot}087$ mm^{-1}, $F(000) = 704$, room temperature, $R = 3{\cdot}4\%$ for 562 observed reflections, m.p. 588 K. The title compound was prepared by the cyclic condensation of four 1-hydroxy-2-naphthoic acid molecules. The tetramer displays $\bar{4}$ molecular symmetry in accordance with its being in a special position on a crystallographic inversion tetrad. The four unique arylcarboxylate units are arranged up and down about the $\bar{4}$ axis. The central sixteen-membered ring is locked in a rigid conformation mainly by intramolecular short contacts involving the carboxylate groups.

Introduction. Intermolecular condensation of 2-hydroxybenzoic acid and of several of its alkylated derivatives (Baker, Gilbert & Ollis, 1951, 1952) leads mainly to cyclic polyesters (salycilides). Several of these compounds are prone to include solvent of crystallization. With a view to studying the potential host properties of isologues of the salycilides, 1-hydroxy-2-naphthalenecarboxylic acid (1-hydroxy-2-naphthoic acid; compound I) was considered an attractive precursor owing to its larger aromatic moiety. By interaction of (I) with phosphorus pentoxide in xylene a complex mixture of products was obtained from which the title compound tetra-1-naphthoide‡ (compound II) was isolated in pure form (8%). (II) forms rather unstable clathrate compounds with most of the usual organic solvents (Suwińska & Gerdil, 1985).

Experimental. A mixture of recrystallized 1-hydroxy-2-naphthoic acid (40·5 g, m.p. 467 K), phosphoric anhydride (42 g) and xylene (500 ml) was boiled under reflux for 6 h. The cooled mixture was washed with water, cold $NaHCO_3$ solution, dried over $MgSO_4$ and evaporated. Powdered orange residue (12·2 g) was refluxed with ethyl acetate (150 ml) for $\frac{1}{2}$ h and solution cooled at *ca* 258 K. Yellow micro-crystalline precipitate (3·2 g) was filtered off and flash-chromatographed on silica gel with toluene/chloroform (1:1) as eluant to yield solvent-free tetranaphthoide (2·8 g) after evaporation of the first fraction under reduced pressure. Pure colourless microcrystalline product obtained by successive recrystallization from benzene followed by desolvation (calc. for $C_{44}H_{24}O_8$: C 77·64, H 3·55; found C 77·49, H 3·61%). Unsolvated well shaped octahedral prisms (m.p. 588–591 K) are grown from ethyl L-lactate.

Colourless crystal of average dimensions 0·18 × 0·30 × 0·30 mm; Philips PW 1100 diffractometer, graphite-monochromated Mo $K\alpha$; cell dimensions from 23 reflections [$2\theta = 21$–$30°$]; data collection: $\sin\theta/\lambda \leq 0{\cdot}53$ Å^{-1}, h 0–13, k 0–13, l 0–10 and all anti-reflections of these, $\omega/2\theta$ scans, ω-scan angle 1·1°; 1029 reflections, 562 with $|F| > 3\sigma(F)$ and $|F| > 7$, Lorentz–polarization, no absorption correction, systematic absences: $hk0$: $h+k = 2n+1$, $00l$: $l = 2n+1$; distribution of data $\langle E^2-1\rangle = 1{\cdot}043$ indicated centrosymmetric space group; structure solved by *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980); full-matrix least squares using $|F|$ values. 118 parameters refined: one scale factor, atomic positional parameters for all atoms (including H atoms), and anisotropic temperature factors for non-H atoms. Isotropic ($U = 0{\cdot}038$ Å^2) H atoms initially placed at 1·09 Å from C atoms. $R = 3{\cdot}4$, $wR = 3{\cdot}4\%$, $S = 3{\cdot}44$, $w(F) = \exp[18{\cdot}0 \times (\sin\theta/\lambda)^2]$ (Dunitz & Seiler, 1973); max. and average $|\Delta|/\sigma$ values for non-H atomic parameters 0·002 and 0·0005 respectively, for H atomic parameters 0·38 and 0·21 respectively; max. and min. heights in final difference electron density map 0·19 and −0·23 e Å^{-3}; atomic scattering factors from Cromer & Waber (1974); all calculations performed with a local version of *XRAY*76 (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976) and *ORTEP*II (Johnson, 1976).

* Systematic name: 7*H*,15*H*,23*H*,31*H*-8,16,24,32-tetraoxacyclohexadeca[1,2-*a*:5,6-*a'*:9,10-*a''*:13,14-*a'''*]tetranaphthalene-7,15,23,31-tetrone.

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‡ For convenience the trival name tetra-1-naphthoide is suggested for the title compound in analogy with other lactides: salicylides, anthranilides *etc.* The intervening number in the trivial name refers to the position of the hydroxy group in the precursor naphthalene-carboxylic acid and so fixes unambiguously the constitution of the naphthoide since *ortho* substitution is a necessary condition for intermolecular condensation to occur.

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Discussion. Final positional parameters and equivalent isotropic temperature factors (for non-hydrogen atoms) are given in Table 1.* Selected molecular parameters are reported in Table 2. The value $Z = 2$ fixes the molecules in the special position on the crystallographic inversion tetrads with four 'planar' $C_{11}H_6O_2$ units (Fig. 1) arranged up and down about the central symmetry axis. These four symmetry-related molecular fragments are bonded together by four *trans* ester linkages giving rise to a central sixteen-membered ring fused to four naphthalene rings. The largest deviation of the naphthalene C atoms from planarity is 0·026 (4) Å. The O(2) atom of the carboxylate group lies at a perpendicular distance of 0·212 (3) Å from the mean aromatic ring. Two naphthalene rings related by a twofold axis are inclined from one another at an angle of 66·8°.

The large ring internal strain is mainly caused by repulsion between the O(1) atoms related by the symmetry operation $\bar{4}$ and separated by 2·626 (3) Å (in the following, most of the steric parameters stressed in the discussion are fourfold). This strain is partly minimized by a concomitant rotational displacement of the carboxylate groups about the C(2)—C(11) bonds (see Table 2). The front strain of the O(1) atoms with the opposite carboxylate group is further exemplified by the short non-bonded distance $O(1^{i})\cdots C(11^{ii}) =$ 2·773 (4) Å. The steric interaction between O(1) atoms related by a twofold axis is very weak at a distance of 3·363 (3) Å. As a whole the sixteen-membered ring is

* Lists of structure factors and anisotropic thermal parameters not involving the H atoms have been deposited with the British Library Division as Supplementary Publication No. SUP 42309 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Fractional coordinates and equivalent isotropic temperature factors* ($Å^2 \times 10^3$) *with e.s.d.'s in parentheses*

(U_{eq} is the average of the eigenvalues of **U**.)

	x	y	z	U_{eq}
O(1)	0·25782 (17)	0·12229 (18)	0·19271 (24)	35·8 (7)
O(2)	0·47801 (24)	0·34728 (23)	0·1651 (3)	57·1 (9)
C(1)	0·33359 (25)	0·1179 (3)	0·0926 (4)	32·6 (10)
C(2)	0·4097 (3)	0·1901 (3)	0·0845 (4)	35·8 (11)
C(3)	0·4785 (3)	0·1865 (3)	−0·0259 (4)	41·8 (11)
C(4)	0·4719 (3)	0·1124 (3)	−0·1246 (4)	43·6 (11)
C(5)	0·3888 (3)	−0·0428 (3)	−0·2153 (4)	43·6 (11)
C(6)	0·3143 (3)	−0·1149 (3)	−0·2046 (4)	47·2 (12)
C(7)	0·2420 (3)	−0·1106 (3)	−0·0991 (4)	50·7 (12)
C(8)	0·2462 (3)	−0·0349 (3)	−0·0017 (4)	42·1 (11)
C(9)	0·3244 (3)	0·0404 (3)	−0·0081 (4)	35·5 (11)
C(10)	0·3949 (3)	0·0373 (3)	−0·1171 (3)	36·8 (10)
C(11)	0·4258 (3)	0·2739 (3)	0·1866 (4)	35·9 (10)
H(3)	0·542 (4)	0·239 (4)	−0·029 (5)	
H(4)	0·527 (4)	0·108 (4)	−0·199 (5)	
H(5)	0·448 (4)	−0·050 (4)	−0·292 (5)	
H(6)	0·311 (4)	−0·172 (4)	−0·284 (5)	
H(7)	0·184 (4)	−0·165 (4)	−0·101 (6)	
H(8)	0·189 (4)	−0·029 (4)	0·081 (6)	

Table 2. *Selected molecular parameters*

The symmetry-related molecular fragments are characterized in Fig. 1. The atoms belonging to fragments other than (i) are further identified by adequate lettering.

Bond distances (Å) with e.s.d.'s in parentheses

O(1)—C(1)	1·393 (4)	C(4)—C(10)	1·416 (5)
O(2)—C(11)	1·202 (5)	C(5)—C(6)	1·366 (5)
C(1)—C(2)	1·381 (5)	C(5)—C(10)	1·424 (5)
C(1)—C(9)	1·418 (5)	C(6)—C(7)	1·399 (6)
C(2)—C(3)	1·404 (5)	C(7)—C(8)	1·374 (6)
C(2)—C(11)	1·497 (5)	C(8)—C(9)	1·428 (5)
C(3)—C(4)	1·370 (5)	C(9)—C(10)	1·408 (5)
		C(11)—O(1^{iv})	1·349 (4)

Bond angles (°) (the upper limit for the e.s.d.'s is 0·3°)

C(11^{iii})—O(1)—C(1)	118·4
O(1)—C(1)—C(2)	121·9
O(1)—C(1)—C(9)	116·8
C(1)—C(2)—C(11)	124·7
C(3)—C(2)—C(11)	116·1
C(2)—C(11)—O(1^{iv})	113·3
C(2)—C(11)—O(2)	123·7

Endocyclic torsion angles (°) of a unique portion of the central ring (the upper limit for the e.s.d.'s is 0·6°)

O(1)—C(1)—C(2)—C(11)	6·0
C(1)—C(2)—C(11)—O(1^{iv})	17·0
C(2)—C(11)—O(1^{iv})—C(1^{iv})	−176·2
C(11)—O(1^{iv})—C(1^{iv})—C(2^{iv})	90·5

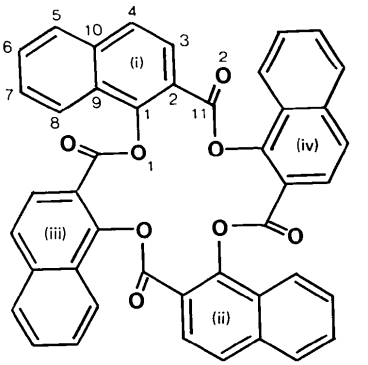

Fig. 1. Atom numbering scheme of the unique part of the molecule, as listed in Table 1. The symmetry-related fragments are generated by the relations: (i) x, y, z; (ii) $\frac{1}{2}-x, \frac{1}{2}-y, z$; (iii) $y, \frac{1}{2}-x, \frac{1}{2}-z$; (iv) $\frac{1}{2}-y, x, \frac{1}{2}-z$.

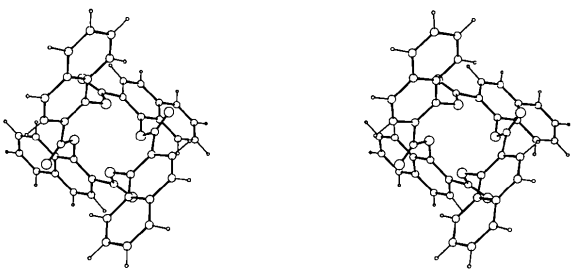

Fig. 2. Stereoview of the molecule in special position on the $\bar{4}$ axis, as viewed down **c**.

locked in a rigid conformation mainly by the aforementioned short contacts involving the carboxylate groups, as well as by the torsional barriers imposed on the ring system by the unsaturated bonds of the naphthalene rings. Indeed, *ortho* substitution brings O(1) in close proximity to C(11), at a distance 2·974 (4) Å, with a minimal torsion of 6° about the unsaturated C(1)–C(2) bond. Fig. 2 shows the molecule viewed down **c**.

There are no noticeable short intermolecular contacts.

References

BAKER, W., GILBERT, B. & OLLIS, W. D. (1951). *J. Chem. Soc.* pp. 201–208.

BAKER, W., GILBERT, B. & OLLIS, W. D. (1952). *J. Chem. Soc.* pp. 1443–1446.

CROMER, D. T. & WABER, J. T. (1974). In *International Tables for X-ray Crystallography*, Vol. IV. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht.)

DUNITZ, J. D. & SEILER, P. (1973). *Acta Cryst.* B**29**, 589–595.

JOHNSON, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee.

MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1980). *MULTAN*80. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain-la-Neuve, Belgium.

STEWART, J. M., MACHIN, P. A., DICKINSON, C. W., AMMON, H. L., HECK, H. & FLACK, H. (1976). The *XRAY*76 system. Tech. Rep. TR446. Computer Science Center, Univ. of Maryland, College Park, Maryland.

SUWIŃSKA, K. & GERDIL, R. (1985). In preparation.

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Structure of 4-Methyl-5-(2-pyrazinyl)-3*H*-1,2-dithiol-3-one: an Oltipraz Analog*

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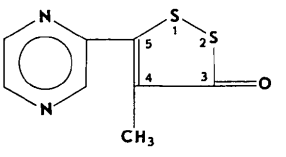
Abstract. $C_8H_6N_2OS_2$, $M_r = 210{\cdot}278$, monoclinic, $P2_1/a$, $a = 11{\cdot}863$ (3), $b = 19{\cdot}873$ (5), $c = 7{\cdot}552$ (3) Å, $\beta = 96{\cdot}01$ (2)°, $V = 1770{\cdot}6$ Å^3, $Z = 8$, $D_m = 1{\cdot}59$ (2), $D_x = 1{\cdot}577$ g cm^{-3}, λ(Mo $K\alpha_1$) = 0·7093 Å, $\mu = 5{\cdot}57$ cm^{-1}, $F(000) = 864$, $T = 296$ (1) K, final $R(F) = 0{\cdot}048$ for 2664 counter data with $F_o^2 \geq 2\sigma(F_o^2)$. As in the case of oltipraz, the two crystallographically independent molecules have corresponding molecular parameters closely resembling each other. Individual six- and five-membered rings are nearly planar to within 0·011 (2) Å, and the angle between plane normals of the six- and five-membered rings is 4·6 (1)° for one molecule and 9·6 (1)° for the other. Bond distances and angles agree well with those found in oltipraz except, of course, for the exocyclic C—O bond distances [av. 1·214 (6) Å].

Introduction. The antischistosomidal drug 4-methyl-5-(2-pyrazinyl)-3*H*-1,2-dithiole-3-thione (oltipraz) acts slowly on mice infected with *Schistosoma mansoni*, and eventually attains parasitological cures by a reduction of the glutathione stores of the parasite (Bueding, Dolan & Leroy, 1982). In their studies, Bueding *et al.* (1982) also used several other drugs, structurally similar to oltipraz, to test and compare their chemotherapeutic values.

As part of our health-related program to provide information regarding structure–function relationships, we have undertaken X-ray structural investigation on drugs of this class containing 3*H*-1,2-dithiole-3-thione as a basic building unit, and the structures of oltipraz (Wei, 1983), 5-(*p*-methoxyphenyl)-3*H*-1,2-dithiole-3-thione (Wang, Lin & Wei, 1985), and 3*H*-1,2-dithiole-3-thione (Wei, 1985) have been elucidated. The title compound (I) possesses a chemical formula closely resembling that of oltipraz but with the thione S replaced by an O. This simple modification of the chemical formula, however, renders the title compound therapeutically inactive. It is informative, therefore, to compare the structure of the title compound with that of oltipraz.



(I)

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