(a)

(b)

Fig. 2. Crystal structures of (a) crystal (I) and (b) crystal (II).

ent between both crystals. The three dihedral angles formed by three benzene rings are similar in both crystals: 72.5 for (I) and 71.9° for (II) between A and B rings, 77.4 for (I) and 73.9° for (II) between A and C rings and 78.3 for (I) and 80.0° for (II) between B and C rings.

The crystal-packing diagrams for both crystals are given in Fig. 2 (PLUTO; Motherwell & Clegg, 1978). In crystal (I), the carbonyl O atom of an acetone molecule makes a hydrogen bond with the hydroxy O atom of the host molecule [O(9)···O(22) = 2.831 (5) Å]. On the other hand, in (II) the carbonyl O atom of the acetone links two host hydroxy O atoms related by a twofold rotation symmetry at (x,y,z) and $(-x,y,\frac{3}{2} - z)$ through two equivalent hydrogen bonds [O(9)···O(22) = 2.901 (3) Å]. The difference in the hydrogen-bond scheme between crystals (I) and (II) is reflected in the difference of the melting points of the two crystals.

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Structure of 2,3-Naphthalenedicarboxylic Acid

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Abstract. $C_{12}H_8O_4$, $M_r = 216.20$, monoclinic, $C2/c$, $a = 5.087$ (2), $b = 19.222$ (3), $c = 9.552$ (2) Å, $\beta = 93.81$ (3)°, $V = 932.0$ (5) Å^3, $Z = 4$, $D_x = 1.54$ g cm^{-3}, $\lambda = 0.71073$ Å, $\mu = 1.09$ cm^{-1}, $F(000) = 488$, $T = 295$ K, $R = 0.037$ for 687 unique reflections having $I > 3\sigma(I)$. In the structure reported here, a twofold axis lies in the plane of the molecule and bisects the three central ring bonds. The average

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C—C bond distance in the naphthalene core is 1.401 (27) Å and the average interior angle 120.0 (14)°. The average deviation of the C atoms comprising the naphthalene rings from the best least-squares plane describing the rings is 0.021 (8) Å. The plane of the single unique carboxylic acid group makes a dihedral angle of 33.1 (1)° with the least-squares plane of the naphthalene core. The carboxylic acid group, in which the observed O—H distance is 1.00 (3) Å, forms a cyclic-dimer hydrogen bond across a center of inversion with the H···O(acceptor) distance 1.68 (3) Å, the O···O-(acceptor) distance 2.676 (2) Å and the O—H···O-(acceptor) angle 174 (3)°. The C—O bond lengths indicate no disorder in the carboxylic acid dimers. The molecules are arranged in stacks with the naphthalene cores parallel to the (102) plane and with the hydrogen bonds of the acid groups linking adjacent stacks. This structure of 2,3-naphthalenedicarboxylic acid is essentially the same as that of o-phthalic acid, but with the b cell edge correspondingly larger to accommodate the additional aromatic ring.

Introduction. The dicarboxylic acids of naphthalene have been of interest to us as part of a continuing investigation of hydrogen bonding in the organic solid state. To date, the crystalline structures of 1,8-naphthalenedicarboxylic acid (Fitzgerald, Gallucci & Gerkin, 1991) and 1,2-naphthalenedicarboxylic acid (Fitzgerald, Gallucci & Gerkin, 1992) have been determined and have shown a variety of hydrogen-bonding arrangements. Here, we describe the results of our investigation of crystalline 2,3-naphthalenedicarboxylic acid, and compare the results to those for 1,8-naphthalenedicarboxylic acid and 1,2-naphthalenedicarboxylic acid.

Experimental. 2,3-Naphthalenedicarboxylic acid, (I), from Aldrich Chemical Company was dissolved in ethanol, mixed with Norit-A decolorizing carbon and subsequently filtered. The diacid thus purified was crystallized from ethanol by slow evaporation at room temperature. The experimental sample was a clear hexagonal plate with approximate principal dimensions $0.13 \times 0.31 \times 0.38$ mm. This was mounted on a glass fiber with epoxy cement and data were collected at room temperature with a Rigaku AFC-5S diffractometer utilizing graphite-monochromated Mo $K\overline{\alpha}$ radiation.

(I)
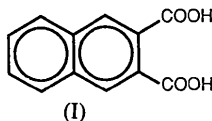
Unit-cell parameters were obtained from a symmetry-restricted least-squares fit of the setting angles for 20 centered reflections with $24 < 2\theta < 30°$. Intensity data were measured for 1232 reflections (exclusive of standards) with $+h$, $+k$, $\pm l$ indices ($h_{max} = 6$, $k_{max} = 24$, $-12 \leq l \leq 12$) and 2θ values in the range $4 \leq 2\theta \leq 55°$. The ω–2θ scan technique was employed with scan widths $(1.6 + 0.35\tan\theta)°$ in ω, and a background/scan time-ratio of 0.5. A variance was assigned to each reflection by means of the formula $\sigma(I)^2 = \sigma_{cs}^2(I) + (0.03I)^2$ in which σ_{cs} is based on counting statistics and I is the integrated intensity. Six standard reflections ($\overline{2}20$, $\overline{1}1\overline{2}$, $11\overline{2}$, $\overline{2}2\overline{6}$, $\overline{2}06$, $1,13,\overline{1}$) were measured after every 150 reflections; over the course of the data collection they showed, on average, a maximum non-systematic relative intensity variation of $\pm 2.9\%$. No correction was made for decay or absorption; the data were corrected for Lorentz and polarization effects. Averaging equivalent reflections gave 1112 independent reflections with $R_{int} = 0.012$.

The crystal system was found to be monoclinic; observed systematic absences (hkl: $h + k = $ odd; $h0l$: $l = $ odd) were consistent with space groups $C2/c$ and Cc. Intensity statistics indicated a centric space group so $C2/c$ (No. 15) was given initial preference and, since refinement proceeded well, it was adopted. The direct-methods program $SHELXS86$ (Sheldrick, 1985) was used to generate an E map from which the initial positions of all non-H atoms were identified. After anisotropic refinement of these atoms converged, Fourier difference methods were used to locate the positions of the H atoms. Full-matrix least-squares refinement (Molecular Structure Corporation, 1989) minimized the function $\sum\sigma(F)^{-2} \times (|F_o| - |F_c|)^2$ in which $\sigma(F) = \sigma(I)/2F\mathrm{Lp}$. Neutral-atom scattering factors and anomalous-dispersion factors were taken from Cromer & Waber (1974) for C and O; the scattering factor for H was taken from Stewart, Davidson & Simpson (1965).

The results of the final refinement cycle were: 687 independent observations having $I > 3\sigma(I)$; 89 variables; $R = 0.037$; $wR = 0.043$; $w = \sigma(F)^{-2}$; $S = 1.51$; $(\Delta/\sigma)_{max} < 0.01$. Maximum and minimum peaks on the final electron density difference map had values 0.22 and -0.16 e Å^{-3}, respectively. The maximum peak was located near (0.03, 0.39, 0.26) approximately half-way along the C(2)—C(2^i) bond; the minimum peak was located near (0.47, 0.05, 0.74) approximately 1.4 Å from C(2), C(3) and C(4). [For the final refinement cycle for 752 independent observations having $I > \sigma(I)$: $R = 0.040$; $wR = 0.044$; $S = 1.48$; $(\Delta/\sigma)_{max} < 0.01$. Similarly, for the final refinement cycle for 950 independent observations having $I > 0$: $R = 0.059$; $wR = 0.046$; $S = 1.36$; $(\Delta/\sigma)_{max} < 0.01$. These latter results are provided for comparison only.]

Final atomic coordinates, equivalent isotropic and isotropic displacement parameters with their e.s.d.'s

are given in Table 1.* In the present study, 2,3-naphthalenedicarboxylic acid crystallized such that a twofold axis lay in the plane of the molecule and bisected the three central naphthalene ring bonds. Fig. 1 shows one complete diacid molecule, two asymmetric units, with selected interatomic distances and angles.

Discussion. An *ORTEPII* (Johnson, 1976) drawing of 2,3-naphthalenedicarboxylic acid (2,3-NDC hereafter) is shown in Fig. 1. Table 2 compares selected values describing the present structure to those of 1,8-naphthalenedicarboxylic acid (1,8-NDC) (Fitzgerald, Gallucci & Gerkin, 1991) and 1,2-naphthalenedicarboxylic acid (1,2-NDC) (Fitzgerald, Gallucci & Gerkin, 1992). Among these diacids, 2,3-NDC contains a crystallographic symmetry element (twofold axis) while 1,8-NDC and both forms of 1,2-NDC do not. For the naphthalene core of 2,3-NDC, the average C—C bond distance, 1.401 (27) Å, and average interior angle, 120.0 (14)°, are very similar to respective values for the other diacids. However, the deviation of the C atoms comprising the respective naphthalene rings from the best least-squares planes describing these rings varies slightly among the diacids. The average deviation for 2,3-NDC is 0.021 (8) Å; 1,8-NDC, with the two carboxylic acid groups at the 'peri' positions of the naphthalene ring, has a larger average deviation from planarity while both forms of 1,2-NDC have comparable deviations. The values of the dihedral angles between the carboxylic acid groups for each structure and the least-squares plane of the respective naphthalene cores are also provided in Table 2. Both acid groups of 2,3-NDC form dihedral angles of 33.1 (1)° with the least-squares plane of the naphthalene core, a disposition quite similar to that exhibited by 1,8-NDC. Among these four diacids, the triclinic form of 1,2-NDC has the smallest average deviation from planarity and an arrangement of the two acid groups that most closely approximates one group being coplanar with the naphthalene rings and one group being perpendicular to the naphthalene rings.

The single unique carboxylic acid group of 2,3-NDC is involved in a cyclic-dimer hydrogen bond across a center of inversion. The O(2)—H(1) distance is 1.00 (3) Å, the O(2)···O(1^i) distance is 2.676 (2) Å, the H(1)···O(1^i) distance is 1.68 (3) Å

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* Lists of structure factors, anisotropic displacement parameters, ring-H-atom coordinates and isotropic displacement parameters, and data pertaining to least-squares best-fit planes have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55298 (13 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: ST0572]

Table 1. *Final positional parameters and equivalent isotropic and isotropic displacement parameters* (Å²) *for 2,3-naphthalenedicarboxylic acid*

O and C atoms were refined anisotropically; $B_{eq} = (8\pi^2/3) \times \Sigma_i \Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$. The H atom was refined isotropically. E.s.d.'s are given in parentheses.

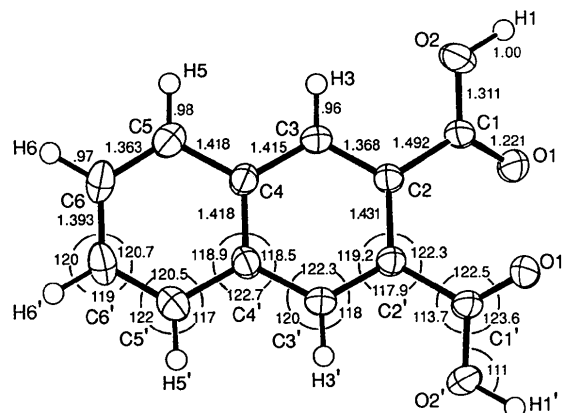|	x	y	z	B_{eq}/B
O(1)	0.0162 (3)	0.27707 (7)	0.1012 (1)	2.91 (6)
O(2)	0.4056 (3)	0.32755 (8)	0.0761 (2)	3.44 (7)
C(1)	0.1697 (4)	0.3253 (1)	0.1235 (2)	2.23 (7)
C(2)	0.0964 (4)	0.3898 (1)	0.1988 (2)	2.02 (7)
C(3)	0.1911 (4)	0.4518 (1)	0.1535 (2)	2.45 (8)
C(4)	0.1002 (4)	0.5165 (1)	0.2019 (2)	2.27 (8)
C(5)	0.1989 (4)	0.5811 (1)	0.1566 (2)	2.99 (10)
C(6)	0.1011 (5)	0.6421 (1)	0.2042 (2)	3.14 (10)
H(1)	0.436 (5)	0.286 (1)	0.015 (3)	6.6 (7)

Fig. 1. An *ORTEPII* (Johnson, 1976) view of 2,3-naphthalenedicarboxylic acid showing the adopted numbering scheme. Displacement ellipsoids have been drawn at 50% probability for all atoms except H, for which they have been set artificially small. Bond lengths (Å) are shown on one asymmetric unit, bond angles (°) on the other. The e.s.d.'s for bond lengths involving C and O atoms are 0.003 Å, for bond angles involving C and O, 0.2°. The e.s.d.'s for the respective values involving H atoms are 0.03 Å and 2°.

and the O(2)—H(1)···O(1^i) angle is 174 (3)°. These values are similar to those for 1,8-NDC and 1,2-NDC (see Table 2). The C—O bond lengths for 2,3-NDC: C(1)—O(1) 1.221 (2) and C(1)—O(2) 1.311 (2) Å, are in agreement, respectively, with the typical values for C—O double bonds and C—O single bonds of aromatic carboxylic acids (Allen, Kennard, Watson, Brammer, Orpen & Taylor, 1987). However, there is a significant variation of C—O bond lengths among the four diacids. The carboxylic acid groups of 1,8-NDC have four nearly equal C—O bond lengths whose average is 1.266 (6) Å. One acid group in triclinic 1,2-NDC has C—O bond lengths of 1.242 (3) and 1.284 (3) Å while the remaining four acid groups (including those of the present structure) average 1.215 (6) Å for the C—O double bond and 1.312 (3) Å for the C—O single bond. Moreover, the difference in C—O bond lengths is paralleled by changes in C—C—O bond

Table 2. *Comparison of selected results from structural determinations of crystalline naphthalenedicarboxylic acids*

Selected results for 1,8-naphthalenedicarboxylic acid (1,8-NDC) (Fitzgerald, Gallucci & Gerkin, 1991), 1,2-naphthalenedicarboxylic acid (1,2-NDC) (Fitzgerald, Gallucci & Gerkin, 1992) and 2,3-naphthalenedicarboxylic acid (2,3-NDC) (present study). For individual values, e.s.d.'s are given within parentheses; for average values, standard deviations are so given.

	1,8-NDC	1,2-NDC (tetragonal)	1,2-NDC (triclinic)	2,3-NDC
Naphthalene ring features				
Average C—C distance in core (Å)	1.396 (30)	1.396 (26)	1.395 (27)	1.401 (27)
Average interior angle in core (°)	119.9 (18)	120.0 (10)	120.0 (10)	120.0 (14)
Average deviation of ring atoms from best least-squares plane (Å)	0.055 (30)	0.013 (7)	0.008 (5)	0.021 (8)
Dihedral angle(s) between ring plane and acid-group plane(s) (°)	42.0 (2) 43.2 (2)	71.3 (2) 20.3 (2)	82.7 (1) 7.6 (2)	33.1 (1)
Acid-group C—O bond lengths (Å)				
C(1)—O(1)	1.263 (4)	1.210 (4)	1.242 (3)	1.221 (2)
C(1)—O(2)	1.270 (4)	1.316 (4)	1.284 (3)	1.311 (2)
C(2)—O(3)	1.260 (4)	1.224 (4)	1.220 (3)	–
C(2)—O(4)	1.273 (4)	1.310 (4)	1.309 (3)	–
Acid-group C—C—O bond angles (°)				
C—C(1)—O(1)	119.3 (3)	125.2 (4)	119.6 (2)	122.5 (2)
C—C(1)—O(2)	117.3 (3)	112.2 (4)	115.5 (2)	113.7 (2)
C—C(2)—O(3)	117.5 (3)	122.6 (4)	122.0 (3)	–
C—C(2)—O(4)	119.2 (3)	114.9 (4)	115.0 (3)	–
Hydrogen and hydrogen-bond parameters				
Inequivalent O—H distances (Å)	0.85 (8); 0.69 (7) 0.87 (6); 0.69 (8)	1.09 (6); 0.95 (5)	1.10 (5); 0.95 (4)	1.00 (3)
Inequivalent O···O(acceptor) distances (Å)	2.618 (4); 2.707 (4)	2.604 (4); 2.683 (4)	2.621 (3); 2.665 (3)	2.676 (2)
Inequivalent H···O(acceptor) distances (Å)	1.77 (8); 2.04 (7) 1.84 (6); 1.93 (8)	1.52 (6); 1.74 (6)	1.53 (4); 1.71 (4)	1.68 (3)
Inequivalent O—H···O (acceptor) angles (°)	172 (7); 162 (9) 174 (5); 176 (10)	170 (4); 176 (5)	176 (4); 178 (3)	174 (3)

angles (Table 2), so that the more nearly equal the C—O bond lengths of a given acid group are, the more nearly equal the C—C—O bond angles become. Upon plotting the difference in bond angle $|\Delta\theta|$ against the difference in bond length $|\Delta r|$ (Fig. 2) in a manner analogous to that of Dieterich, Paul & Curtin (1974), we find a nearly linear relation between the two parameters. These differences in the carboxylic acid group conformations, arising from various degrees of disorder, occur even though the hydrogen-bond lengths and angles among the diacids are quite similar, in agreement with Currie, Speakman & Curry (1967). It is important to note, however, that while Dieterich, Paul & Curtin (1974) and Currie, Speakman & Curry (1967) attribute the disorder of the carboxylic acids to alternate orientations:

we have found no evidence of this orientational disorder in analyzing the displacement parameters of the O atoms in 1,8-NDC (Fitzgerald, Gallucci & Gerkin, 1991). We propose that the H atoms disorder by means of rapid oscillations that take place in a double minimum potential (tunnelling).

Fig. 3 presents a stereoview of a unit cell for 2,3-NDC with several additional molecules included in order to illustrate packing arrangements. The long dimension of the 2,3-NDC molecules is parallel to the **b** direction since the twofold axes of the space group (*C2/c*) are coincident with each molecule. The molecules are arranged in stacks with the naphthalene cores nearly parallel to the (102) plane, and are separated by a distance equal to one half of the *c*-axis length. The acid groups, rotated out of the plane of the naphthalene rings, connect adjacent stacks through cyclic-dimer hydrogen bonding across
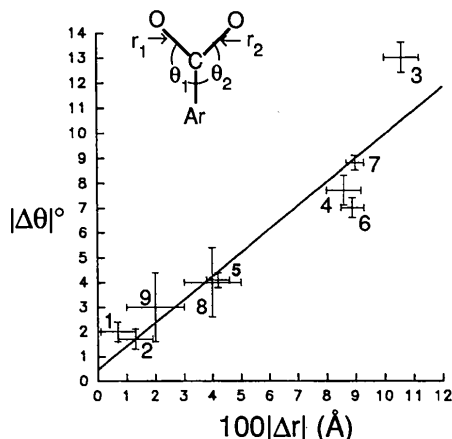

Fig. 2. A plot of $|\Delta\theta|$ *vs* $100|\Delta r|$, after Dieterich, Paul & Curtin (1974), for the acid groups of four dicarboxylic acids of naphthalene: (1), (2) 1,8-NDC (Fitzgerald, Gallucci & Gerkin, 1991); (3), (4) 1,2-NDC (tetragonal) and (5), (6) 1,2-NDC (triclinic) (Fitzgerald, Gallucci & Gerkin, 1992); (7) present study; (8), (9) 1,4-NDC (Derissen, Timmermans & Schoone, 1979).
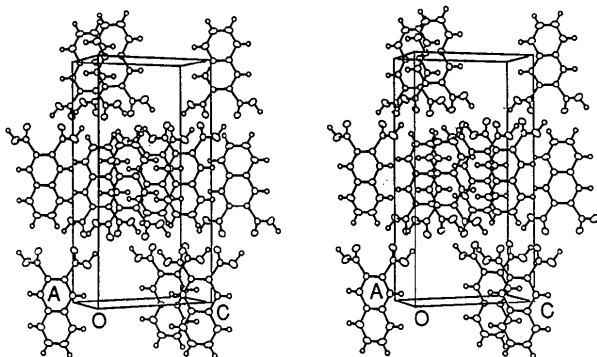

Fig. 3. A stereoview of a unit cell for 2,3-naphthalenedicarboxylic acid drawn using *ORTEP*II (Johnson, 1976). Several molecules in addition to the unit-cell contents have been drawn in order to illustrate the hydrogen bonding and packing arrangements.

inversion centers, thus producing a zigzag pattern along the [10$\bar{1}$] direction. Comparison of the unit-cell dimensions and packing arrangements for 2,3-NDC to those of o-phthalic acid (Ermer, 1981; Küppers, 1981) shows very close agreement in most details, excepting the b cell-edge lengths: 19.222 (3) Å for 2,3-NDC; 14.287 (3) Å for phthalic acid. In the present case, the length of the additional aromatic ring is accommodated by the larger b cell edge.

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Structure of 9-Epiquinine Hydrochloride Dihydrate versus Antimalarial Activity

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Abstract. 9-Epiquinine hydrochloride dihydrate [(9S)-6′-methoxycinchonan-9-ol hydrochloride dihydrate], $C_{20}H_{25}N_2O_2^+.Cl^-.2H_2O$, $M_r = 396.9$, orthorhombic, $P2_12_12_1$, $a = 8.059$ (2), $b = 11.537$ (3), $c = 22.311$ (6) Å, $V = 2074.1$ (9) Å^3, $Z = 4$, $D_x = 1.271$ g cm^{-3}, Cu Kα, $\lambda = 1.54178$ Å, $\mu = 18.58$ cm^{-1}, $F(000) = 848$, room temperature, final $R = 6.56\%$ for 1344 reflections with $|F_o| > 3\sigma(F)$. 9-Epiquinine crystallized as a hydrated tertiary amine hydrochloride salt. The intramolecular N(1)$^+$···O distance is 2.816 Å. All H atoms attached to O or N atoms form intermolecular hydrogen bonds. The Cl ion is involved in four hydrogen bonds including one with the hydroxyl group of 9-epiquinine. The N(1)$^+$—H moiety hydrogen bonds to a water molecule. The O(12)—C(9)···N(1)$^+$—H(1) torsion angle was equal to −0.2 (3.8)° in comparison to 97.0° for quinidine sulfate [Karle & Karle (1981). Proc. Natl Acad. Sci. USA, 78, 5938–5941]. Two theories have been proposed in the literature to explain the low antimalarial activity of 9-epiquinine. The crystal structure of 9-epiquinine hydrochloride is not consistent with the hypothesis that 9-epiquinine prefers to form intramolecular rather than intermolecular hydrogen bonds, but is consistent with the hypothesis that N(1) and the hydroxyl group of 9-epiquinine are in an orientation which is unfavorable towards exerting antimalarial activity.

Introduction. 9-Epiquinine is the epimer of the erythro antimalarial agents quinine and quinidine (Fig. 1). An erythro compound is a compound

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