ORGANIC COMPOUNDS

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3,5-Dimethoxybenzoic Acid and the Second Polymorph of the 2:1 Adduct of 3,5-Dinitrobenzoic Acid with Ethylenediamine

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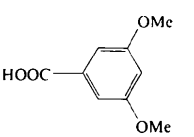
Abstract

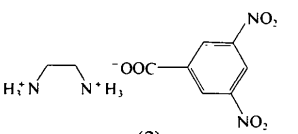
3,5-Dimethoxybenzoic acid, $C_9H_{10}O_4$, is planar and forms hydrogen-bonded cyclic dimers [O···O = 2.644 (2) Å]. The second (monoclinic) polymorph of the 2:1 adduct of 3,5-dinitrobenzoic acid with ethylenediamine, ethylenediammonium 3,5-dinitrobenzoate, $C_2H_{10}N_2^{2+}.2C_7H_3N_2O_6^-$ [$(DNBA)_2^-(en)^{2+}$], is structurally identical to the previously reported triclinic form. It forms a 12-membered hydrogen-bonded ring involving the carboxylate groups of the acids and the protonated amine groups of ethylenediamine. Hydrogen-bond distances (O···N) are 2.678 (2) and 2.729 (2) Å. A nitro group is also involved in a longer intermolecular interaction with an amine group [O···N = 2.898 (2) Å].

Comment

A program of investigation into hydrogen-bonding modes in cocrystalline adducts of aromatic acids with nitrogen bases has now been extended to include polyfunctional aliphatic examples, *e.g.* ethylenediamine (en). Previous studies using ethylenediamine with carboxylic acids (Perez, 1976, 1977; Fair & Schlemper, 1977; Gavrushenko, Carrell, Stallings & Glusker, 1977; Palmer & Ladd, 1977; Stallings, Blount, Srere & Glusker, 1979; Daly, Schonholzer, Behr & Lehn, 1981; Moritani & Kashino, 1991) indicate the ease of protonation of both amine groups. Our studies have shown that whenever an amine is protonated in adduct formation, there are usually three hydrogen bonds involved. If ethylenediamine forms an adduct with a nitro-substituted benzoic acid, then the possibility of hydrogen-bond formation involving a nitro group also is quite likely. Such interactions may, therefore, lead to non-centrosymmetric packing, as found in the structure of 3,5-dinitrobenzoic acid with 4-aminobenzoic acid (Etter & Frankenbach, 1989). In the past, nitro-substituted benzoic acids have been useful in the formation of cocrystalline adducts with aromatic bases. Another class of substituted benzoic acid which has been studied extensively is the dimethoxybenzoic acid series, *e.g.* 2,6-dimethoxybenzoic acid (Bryan & White, 1982*a*; Frankenbach, Britton & Etter, 1991). These are of particular interest because the carboxylic acid group which is non-coplanar with the ring gives an unusual chain pattern of hydrogen bonds. The structures of the 2,3- and 3,4-dimethoxy-substituted acids are also known (Bryan & White, 1982*b*; Swaminathan, Vimala & Lessinger, 1975). However, no structures of adducts involving this acid have yet been reported. Reported here are the crystal structures of 3,5-dimethoxybenzoic acid (DMBA), (1), and the 2:1 adduct of 3,5-dinitrobenzoic acid (DNBA) with ethylenediamine [$(DNBA)_2^-(en)^{2+}$], (2). Although the structure of a triclinic modification of the latter adduct has been reported (Nethaji, Pattabhi, Chhabra & Poonia, 1992), it was decided to complete the structure of our monoclinic polymorph to compare the inherent hydrogen-bonding modes.



(1)



(2)

The structure of 3,5-dimethoxybenzoic acid (DMBA), (1), is relatively stereotypical, having the general features of most other non-sterically hindered substituted benzoic acids (Fig. 1). As in the case of 3,4-dimethoxybenzoic acid, DMBA is both planar and forms hydrogen-bonded cyclic dimers across a centre of symmetry in the cell. [O(10)···O(11) $(2-x, -y, 1-z)$ 2.644 (2) Å; graph set $R_2^2(8)$ (Etter, 1990)]. Relevant torsion angles C(2)—C(1)—C(11)—O(11), C(4)—C(3)—O(31)—C(31) and C(6)—C(5)—O(51)—C(51) are −1.4 (2), −3.0 (3) and −0.1 (2)°, respectively. The structure of (2) comprises a 2:1 adduct of 3,5-dinitrobenzoic acid and ethylenediamine involved in a three-dimensional hydrogen-bonded network. The two DNBA molecules are

related by crystallographic inversion symmetry. The protons from the carboxylic acid groups of both DNBA molecules are located on the two amino groups of ethylenediamine (Fig. 2). This structure is essentially identical to that of the triclinic modification (Nethaji *et al.*, 1992). It must be assumed that the difference in crystal morphology is due to the different methods employed in the formation and crystallization of the respective adducts. As expected, there are three hydrogen bonds, one to each carboxylate O atom [N(1*B*)···O(10*A*) ($x-1$, y, z) 2.729 (2), N(1*B*)···O(11*A*) ($-x$, $3-y$, $1-z$) 2.678 (2) Å] and one to a nitro O atom [N(1*B*)···O(32*A*)($x-1$, $y+1$, z) 2.898 (2) Å]. The hydrogen bonding between the carboxylate groups and the amines results in a cyclic 12-membered hydrogen-bonded ring [graph set $R_4^4(12)$ (Etter, 1990)]. This ring system is identical to that found in the structures of the 1:1 adduct of 4-aminobenzoic acid with (2,4-dichlorophenoxy)acetic acid (Lynch, Smith, Byriel & Kennard, 1992*a*) and the 3:1:1 adduct of 4-aminobenzoic acid with 2,4,6-trinitrobenzoic acid and 1,3,5-trinitrobenzene (Lynch, Smith, Byriel & Kennard, 1992*b*). In both examples, one 4-amino group is protonated.

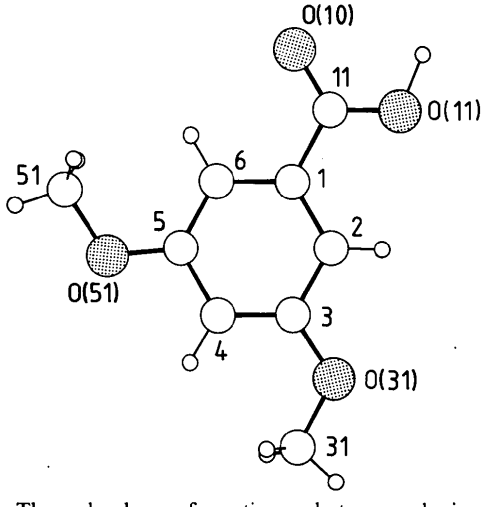


Fig. 1. The molecular conformation and atom-numbering scheme for (1). Unless otherwise indicated, atoms are C atoms.

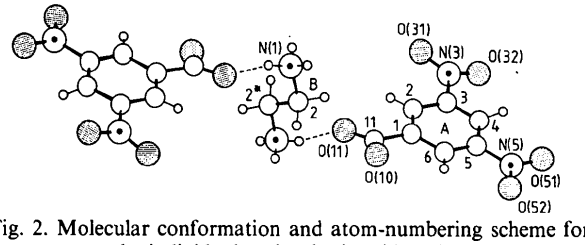


Fig. 2. Molecular conformation and atom-numbering scheme for the individual molecules in adduct (2).

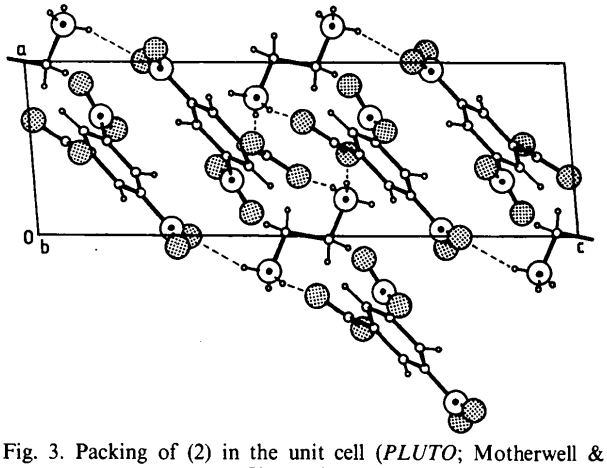


Fig. 3. Packing of (2) in the unit cell (*PLUTO*; Motherwell & Clegg, 1978).

Experimental

3,5-Dimethoxybenzoic acid (1) was obtained from the ethanolic solution used in the attempted preparation of the 1:1 adduct of 3,5-dimethoxybenzoic acid (DMBA) and 2-aminopyrimidine in ethanol. Both a white powder (m.p. 399–403 K) and colourless prisms (m.p. 459–463 K) formed upon total evaporation of the solvent at room temperature. Compound (2) was prepared by dissolving a 2:1 molar ratio of 3,5-dinitrobenzoic acid (DNBA) and ethylenediamine (en) in hot aqueous ethanol (*ca* 353 K). Large yellow prisms (m.p. 509.5–511 K) formed upon partial evaporation of the solvents at room temperature (*cf.* pale green crystals of the triclinic modification).

Compound (1)

Crystal data

$C_9H_{10}O_4$
M_r = 182.2
Monoclinic
$P2_1/c$
a = 10.879 (4) Å
b = 4.9238 (3) Å
c = 16.388 (6) Å
β = 104.42 (2)°
V = 850.2 (4) Å^3
Z = 4
D_x = 1.423 Mg m^{-3}
Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 25 reflections
θ = 6–14°
μ = 0.11 mm^{-1}
T = 295 K
Prismatic
0.44 × 0.24 × 0.18 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
$2\theta/\omega$ scans
Absorption correction: empirical
T_{min} = 0.985, T_{max} = 0.998
1777 measured reflections
1492 independent reflections
1122 observed reflections [$I > 2.5\sigma(I)$]
R_{int} = 0.008
θ_{max} = 25°
h = 0 → 12
k = 0 → 5
l = −19 → 19
3 standard reflections monitored every 250 reflections
intensity variation: 0.4%

Refinement

Refinement on F
$R = 0.032$
$wR = 0.035$
$S = 1.40$
1122 reflections
118 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o) + 5.20 \times 10^{-4}(F_o)^2]$
$(\Delta/\sigma)_{max} = 0.03$
$\Delta\rho_{max} = 0.13$ e Å^{-3}
$\Delta\rho_{min} = -0.16$ e Å^{-3}
Atomic scattering factors from *SHELXS*86 (Sheldrick, 1985)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2) *for* (1)

$U_{eq} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
C(1)	0.7883 (1)	0.4906 (3)	0.4095 (1)	0.0331 (5)
C(11)	0.8811 (2)	0.2805 (3)	0.4504 (1)	0.0344 (5)
O(10)	0.9774 (1)	0.2358 (3)	0.4244 (1)	0.0464 (4)
O(11)	0.8567 (1)	0.1498 (3)	0.5130 (1)	0.0454 (4)
C(2)	0.6795 (2)	0.5381 (3)	0.4364 (1)	0.0355 (5)
C(3)	0.5937 (2)	0.7343 (3)	0.3954 (1)	0.0352 (5)
O(31)	0.4892 (1)	0.7703 (3)	0.4257 (1)	0.0463 (4)
C(31)	0.4021 (2)	0.9789 (5)	0.3881 (1)	0.0470 (7)
C(4)	0.6171 (2)	0.8783 (4)	0.3284 (1)	0.0370 (5)
C(5)	0.7275 (2)	0.8278 (3)	0.3025 (1)	0.0362 (5)
O(51)	0.7406 (1)	0.9813 (3)	0.2358 (1)	0.0507 (5)
C(51)	0.8504 (2)	0.9413 (6)	0.2052 (2)	0.0607 (9)
C(6)	0.8138 (2)	0.6352 (4)	0.3422 (1)	0.0366 (5)

Table 2. *Selected geometric parameters* (Å, °) *for* (1)

C(11)—C(1)	1.484 (2)	C(2)—C(1)	1.382 (3)
C(6)—C(1)	1.397 (3)	O(10)—C(11)	1.245 (2)
O(11)—C(11)	1.293 (2)	C(3)—C(2)	1.394 (2)
O(31)—C(3)	1.362 (2)	C(4)—C(3)	1.382 (3)
C(31)—O(31)	1.429 (2)	C(5)—C(4)	1.392 (3)
O(51)—C(5)	1.366 (2)	C(6)—C(5)	1.379 (2)
C(51)—O(51)	1.419 (3)		
C(2)—C(1)—C(11)	120.9 (2)	C(6)—C(1)—C(11)	117.7 (2)
C(6)—C(1)—C(2)	121.3 (1)	O(10)—C(11)—C(1)	120.3 (2)
O(11)—C(11)—C(1)	117.0 (2)	O(11)—C(11)—O(10)	122.7 (1)
C(3)—C(2)—C(1)	119.1 (2)	O(31)—C(3)—C(2)	115.7 (2)
C(4)—C(3)—C(2)	120.4 (2)	C(4)—C(3)—O(31)	124.0 (1)
C(31)—O(31)—C(3)	117.4 (1)	C(5)—C(4)—C(3)	119.6 (2)
O(51)—C(5)—C(4)	114.5 (1)	C(6)—C(5)—C(4)	121.1 (2)
C(6)—C(5)—O(51)	124.3 (2)	C(51)—O(51)—C(5)	118.1 (2)
C(5)—C(6)—C(1)	118.5 (2)		

Compound (2)

Crystal data

$C_2H_{10}N_2^{2+}.2C_7H_3N_2O_6^-$
$M_r = 484.3$
Monoclinic
$P2_1/c$
$a = 5.505$ (3) Å
$b = 10.699$ (1) Å
$c = 17.55$ (1) Å
$\beta = 95.15$ (2)°
$V = 1029.5$ (8) Å^3
$Z = 2$
$D_x = 1.562$ Mg m^{-3}
Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 25 reflections
$\theta = 6$-14°
$\mu = 0.13$ mm^{-1}
$T = 295$ K
Prismatic
0.34 × 0.32 × 0.26 mm
Yellow

Data collection

Enraf-Nonius CAD-4 diffractometer
$R_{int} = 0.022$
$\theta_{max} = 25°$
$2\theta/\omega$ scans
Absorption correction: empirical
$T_{min} = 0.966$, $T_{max} = 0.999$
2141 measured reflections
1817 independent reflections
1410 observed reflections [$I > 2.5\sigma(I)$]
$h = 0 \rightarrow 6$
$k = 0 \rightarrow 12$
$l = -20 \rightarrow 20$
3 standard reflections monitored every 250 reflections
intensity variation: 0.2%

Refinement

Refinement on F
$R = 0.037$
$wR = 0.045$
$S = 0.61$
1410 reflections
186 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o) + 1.08 \times 10^{-2}(F_o)^2]$
$(\Delta/\sigma)_{max} = 0.01$
$\Delta\rho_{max} = 0.16$ e Å^{-3}
$\Delta\rho_{min} = -0.26$ e Å^{-3}
Atomic scattering factors from *SHELXS*86 (Sheldrick, 1985)

Table 3. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2) *for* (2)

$U_{eq} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
C(1*A*)	0.5260 (3)	1.1381 (1)	0.3919 (1)	0.0353 (5)
C(11*A*)	0.4624 (3)	1.2543 (2)	0.4356 (1)	0.0431 (5)
O(10*A*)	0.5313 (3)	1.3555 (1)	0.4119 (1)	0.0703 (6)
O(11*A*)	0.3416 (3)	1.2359 (1)	0.4916 (1)	0.0624 (5)
C(2*A*)	0.4015 (3)	1.0273 (2)	0.4014 (1)	0.0349 (5)
C(3*A*)	0.4583 (3)	0.9232 (1)	0.3599 (1)	0.0338 (5)
N(3*A*)	0.3195 (3)	0.8074 (1)	0.3676 (1)	0.0407 (5)
O(31*A*)	0.1318 (3)	0.8136 (1)	0.3996 (1)	0.0599 (5)
O(32*A*)	0.3967 (3)	0.7109 (1)	0.3413 (1)	0.0503 (4)
C(4*A*)	0.6400 (3)	0.9230 (1)	0.3104 (1)	0.0367 (5)
C(5*A*)	0.7632 (3)	1.0343 (2)	0.3039 (1)	0.0359 (5)
N(5*A*)	0.9610 (3)	1.0368 (2)	0.2526 (1)	0.0427 (5)
O(52*A*)	1.0699 (2)	1.1347 (1)	0.2454 (1)	0.0639 (5)
O(51*A*)	1.0087 (3)	0.9406 (1)	0.2200 (1)	0.0563 (5)
C(6*A*)	0.7097 (3)	1.1421 (2)	0.3423 (1)	0.0378 (5)
N(1*B*)	−0.2085 (3)	1.5728 (1)	0.4229 (1)	0.0358 (5)
C(2*B*)	0.0218 (3)	1.5233 (2)	0.4607 (1)	0.0393 (5)

Table 4. *Selected geometric parameters* (Å, °) *for* (2)

C(11*A*)—C(1*A*)	1.517 (2)	C(2*A*)—C(1*A*)	1.387 (2)
C(6*A*)—C(1*A*)	1.393 (2)	O(10*A*)—C(11*A*)	1.232 (2)
O(11*A*)—C(11*A*)	1.251 (2)	C(3*A*)—C(2*A*)	1.383 (2)
N(3*A*)—C(3*A*)	1.468 (2)	C(4*A*)—C(3*A*)	1.383 (2)
O(31*A*)—N(3*A*)	1.221 (2)	O(32*A*)—N(3*A*)	1.222 (2)
C(5*A*)—C(4*A*)	1.380 (2)	N(5*A*)—C(5*A*)	1.474 (2)
C(6*A*)—C(5*A*)	1.382 (2)	O(52*A*)—N(5*A*)	1.219 (2)
O(51*A*)—N(5*A*)	1.218 (2)	C(2*B*)—N(1*B*)	1.475 (2)
C(2*B*)—C(2*B*^{i})	1.507 (3)		
C(2*A*)—C(1*A*)—C(11*A*)	120.0 (2)	C(6*A*)—C(1*A*)—C(11*A*)	120.2 (1)
C(6*A*)—C(1*A*)—C(2*A*)	119.8 (1)	O(10*A*)—C(11*A*)—C(1*A*)	117.2 (2)
O(11*A*)—C(11*A*)—C(1*A*)	115.6 (2)	O(11*A*)—C(11*A*)—O(10*A*)	127.2 (2)
C(3*A*)—C(2*A*)—C(1*A*)	119.2 (1)	N(3*A*)—C(3*A*)—C(2*A*)	119.1 (1)
C(4*A*)—C(3*A*)—C(2*A*)	122.9 (1)	C(4*A*)—C(3*A*)—N(3*A*)	118.0 (1)
O(31*A*)—N(3*A*)—C(3*A*)	117.7 (1)	O(32*A*)—N(3*A*)—C(3*A*)	118.4 (1)
O(32*A*)—N(3*A*)—O(31*A*)	123.9 (1)	C(5*A*)—C(4*A*)—C(3*A*)	116.1 (1)
N(5*A*)—C(5*A*)—C(4*A*)	117.5 (1)	C(6*A*)—C(5*A*)—C(4*A*)	123.5 (1)
C(6*A*)—C(5*A*)—N(5*A*)	118.9 (1)	O(52*A*)—N(5*A*)—C(5*A*)	118.5 (1)
O(51*A*)—N(5*A*)—C(5*A*)	118.3 (1)	O(51*A*)—N(5*A*)—O(52*A*)	123.3 (1)
C(5*A*)—C(6*A*)—C(1*A*)	118.5 (1)	N(1*B*)—C(2*B*)—C(2*B*^{i}))	109.2 (1)

Symmetry code: (i) $-x, 3-y, 1-z$.

The triclinic cell parameters [a = 6.737 (1), b = 1.803 (7), c = 10.444 (1) Å, α = 94.767 (8), β = 108.30 (1), γ = 97.43 (1) °, V = 512.4 (2) Å^3 (Nethaji *et al.*, 1992)] could not be transformed to our primitive monoclinic cell using standard cell-reduction programs. The data were corrected for Lorentz and polarization effects. The structures were solved by direct methods using *SHELXS*86 (Sheldrick, 1985) and refined by full-matrix least squares (*SHELX*76; Sheldrick, 1976) with anisotropic displacement parameters for all non-H atoms.

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Lists of structure factors, anisotropic displacement parameters and H-atom coordinates have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71807 (15 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: HL1043]

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2′,3′-Didehydro-2′,3′-dideoxy-5-hydroxymethyluridine

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Abstract

The furanose ring in $C_{10}H_{12}N_2O_5$ adopts the O(4′)-*endo* envelope conformation (^0E) and the glycosidic torsion angle C(2)—N(1)—C(1′)—O(4′), χ, is 245.2 (3)°. The pseudorotational parameters are P = 102.7° and τ_m = 5.2°. The CH_2OH group on C(5′) has the t conformation [γ = 179.2 (2)°].

Comment

A number of 2′,3′-dideoxyribonucleosides and 2′,3′-didehydro-2′,3′-dideoxyribonucleosides are potent inhibitors of the human immunodeficiency virus (HIV), the etiological agent of acquired immunodeficiency syndrome (AIDS). 3′-Azido-3′-deoxythymidine (AZT) is used extensively for the treatment of AIDS and AIDS-Related Complex (Broder, Mitsuya, Yarchoan & Pavlakis, 1990; De Clercq, 1991; Yarchoan, Pluda, Perno, Mitsuya & Broder, 1991). 2′,3′-Didehydro-2′,3′-dideoxythymidine (D4T) has been reported to have a comparable potency to AZT against HIV (Baba *et al.*, 1987; Lin, Schinazi & Prusoff, 1987; Mansuri *et al.*, 1989).

5-Hydroxymethyl-2′-deoxyuridine (HMdUrd) is a novel antimetabolite with broad-spectrum antiviral activity (Gupta *et al.*, 1992; Shiau, Shinazi, Chen & Prusoff, 1988) and low systemic toxicity (Meldrum, Gupta, Lowes & Paterson, 1985). HMdUrd-5′-monophosphate is a good inhibitor of thymidylate synthase (Kempf, Barfknecht, Shaffer, Osaki &