Acta Cryst E CRYSTALLOGRAPHIC COMMUNICATIONS

ISSN 2056-9890

Crystal structures of two different multi-component crystals consisting of 1-(3,4-dimethoxybenzyl)-6,7-dimethoxyisoquinoline and fumaric acid

Hiroki Shibata,[a,b]* Aya Sakon,[c] Noriyuki Takata[d] and Hiroshi Takiyama[b]

[a]Pharmaceutical Technology Division, Analytical Development Department, Chugai Pharmaceutical Co. Ltd., 5-5-1 Ukima, Kita-ku, Tokyo 115-8543, Japan, [b]Department of Applied Physics and Chemical Engineering, Tokyo University of Agriculture and Technology, 2-24-16 Naka-cho, Koganei, Tokyo 184-8588, Japan, [c]Pharmaceutical Technology Division, Formulation Development Department, Chugai Pharmaceutical Co. Ltd., 216 Totsuka-cho, Totsuka-ku, Yokohama, Kanagawa 244-8602, Japan, and [d]Manufacturing Technology Division, Quality Development Department, Chugai Pharma Manufacturing Co. Ltd., 2500 Takayanagi, Fujieda, Shizuoka 426-0041, Japan. *Correspondence e-mail: shibata.hiroki63@chugai-pharm.co.jp

Received 13 August 2024
Accepted 7 October 2024

Edited by Y. Ozawa, University of Hyogo, Japan

Keywords: crystal structure; fumaric acid; papaverine; multi-component crystal.

CCDC references: 2312143; 2312144

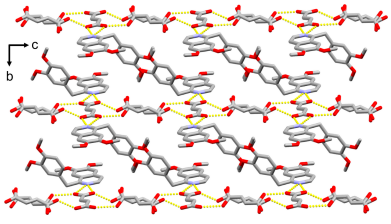
Supporting information: this article has supporting information at journals.iucr.org/e

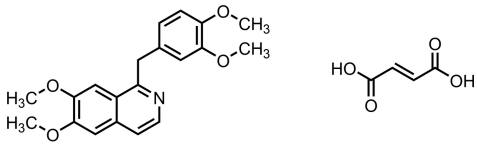
Two different multi-component crystals consisting of papaverine [1-(3,4-dimethoxybenzyl)-6,7-dimethoxyisoquinoline, $C_{20}H_{21}NO_4$] and fumaric acid [$C_4H_4O_4$] were obtained. Single-crystal X-ray structure analysis revealed that one, $C_{20}H_{21}NO_4{\cdot}1.5C_4H_4O_4$ (I), is a salt co-crystal composed of salt-forming and non-salt-forming molecules, and the other, $C_{20}H_{21}NO_4{\cdot}0.5C_4H_4O_4$ (II), is a salt–co-crystal intermediate (*i.e.*, in an intermediate state between a salt and a co-crystal). In this study, one state (crystal structure at 100 K) within the salt–co-crystal continuum is defined as the 'intermediate'.

1. Chemical context

Papaverine (1-[3,4-dimethoxybenzyl]-6,7-dimethoxyisoquinoline) is an isoquinoline alkaloid compound extracted from the mature seed capsules of poppies (Kang *et al.*, 2018). It is an antispasmodic and vasodilator, used primarily in the treatment of smooth muscle spasms and for vasodilation and improvement of symptoms in acute arterial embolism, acute pulmonary embolism, peripheral circulatory disturbance, and coronary circulatory disturbance. The active pharmaceutical ingredient papaverine has been developed as a hydrochloride salt whose crystal structure has been determined (Reynolds *et al.*, 1974). In the pharmaceutical industry, studies on salt crystallization and co-crystallization are conducted for purposes such as improving the solid-state stability of the active pharmaceutical ingredient or improvement of its dissolution properties. Fumaric acid is a dicarboxylic acid and a *cis–trans* isomer of maleic acid and is used in the pharmaceutical industry as a counter-ion in salts and as a conformer of co-crystals. For example, among 1372 new drugs approved by the US Food and Drug Administration between 1939 and 2020, fumaric acid was used as a counter-ion in the salts of ten drugs (Bharate *et al.*, 2021). The recently developed COVID-19 antiviral drug substance Ensitrelvir is crystallized as a co-crystal with fumaric acid (Kawajiri *et al.*, 2023).

In this work, we synthesized two multicomponent crystals — a salt co-crystal (I) and a salt–co-crystal intermediate (II) — consisting of papaverine **1** and fumaric acid **2**, and we determined their crystal structures. In this study, one state (crystal structure at 100 K) within the salt–co-crystal continuum is defined as the 'intermediate'.





Compound (I): **1**·1.5 **2**
Compound (II): **1**·0.5 **2**

2. Structural commentary

The crystal structure of (I) is shown in Fig. 1. It crystallized with a 1:1.5 papaverine:fumaric acid stoichiometric ratio in the space group $P\overline{1}$ with Z = 2, with one full molecule of papaverine and three half molecules of fumaric acid (fumaric acids *A*, *B*, and *C*) in the asymmetric unit. The three fumaric acid molecules were positioned on a center of symmetry, with molecules *A* and *C* being disordered over two positions (O39/O40/C41 and C33).

Since the C30—O31 and C30—O32 distances of fumaric acid molecule *A* are 1.248 (2) Å and 1.246 (3) Å, respectively, the carboxy group of molecule *A* is dissociated (Childs *et al.*, 2007; Chen *et al.*, 2012). In addition, N1 of the papaverine molecule is protonated and is engaged in N—H···O hydrogen bonding (Table 1). Therefore, it was determined that fumaric acid molecule *A* and the papaverine molecule form a salt. The fumaric acid molecules *B* and *C* are hydrogen-bonded to fumaric acid molecule *A*. The C34—O35 and C34—O36 distances in fumaric acid molecule *B* are 1.324 (3) Å and 1.211 (2) Å, respectively, thus the carboxy group of molecule *B* is not dissociated. The C38—O39*A* and C38—O40*A* distances in fumaric acid molecule *C* are 1.280 (5) Å and 1.231 (6) Å, respectively, thus the carboxy group of molecule *C* is not dissociated (Childs *et al.*, 2007; Chen *et al.*, 2012). Therefore, this multicomponent crystal includes both salt-forming and non–salt-forming molecules and was thus concluded to be a salt co-crystal, (I).

Table 1
Hydrogen-bond geometry (Å, °) for (I).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···O31	0.88	2.20	3.034 (3)	159
N1—H1···O32	0.88	2.18	2.919 (2)	141
O35—H35···O31	0.84	1.83	2.617 (2)	156
O39*A*—H39*A*···O32	0.84	1.67	2.502 (4)	169

Table 2
Hydrogen-bond geometry (Å, °) for (II).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O31—H31···N1	0.84 (1)	1.73 (1)	2.5687 (12)	175 (1)
C9—H9···O32^{i}	0.95 (1)	2.27 (1)	3.2191 (14)	176 (1)

Symmetry code: (i) $-x+1, -y+2, -z+1$.

The crystal structure of (II) is given in Fig. 2. It crystallized with a 1:0.5 papaverine:fumaric acid stoichiometric ratio in space group $P2_1/n$ with Z = 4, with one full molecule of papaverine and half a molecule of fumaric acid in the asymmetric unit. The fumaric acid molecule is positioned on the center of symmetry. The C30–O31 and C30–O32 distances in the fumaric acid molecule are 1.306 (1) and 1.223 (1) Å, respectively, indicating that the carboxylic acid of the fumaric acid molecule is not dissociated (Childs *et al.*, 2007; Chen *et al.*, 2012). Therefore, the fumaric acid and papaverine molecules were determined to form a co-crystal. However, the O—H···N hydrogen bond [$D\cdots A$ = 2.5687 (12) Å, Table 2) is

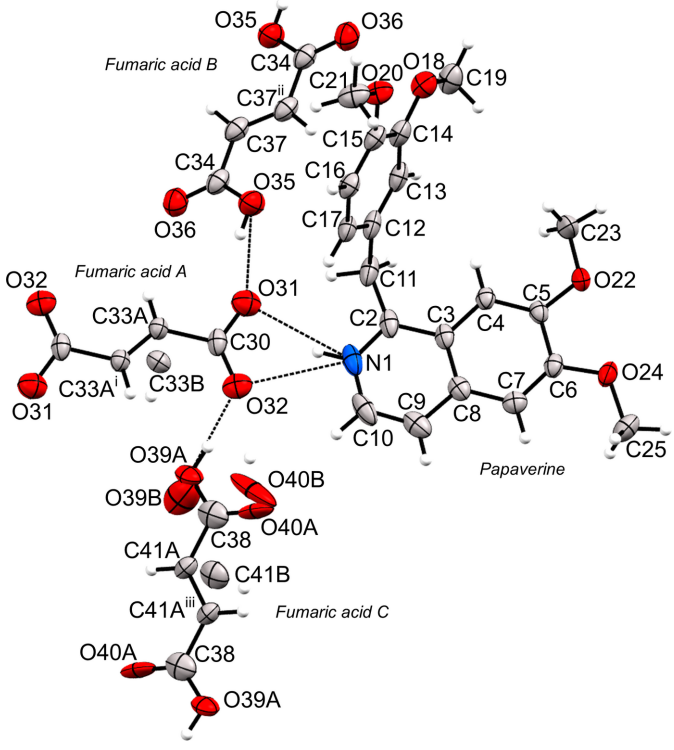


Figure 1
The molecular structure of (I). Hydrogen bonds are shown as dashed lines and displacement ellipsoids are drawn at the 50% probability level. [Symmetry codes: (i) $-x+2, -y+2, -z+1$; (ii) $-x+1, -y+2, -z$; (iii) $-x+2, -y+2, -z+2$.]

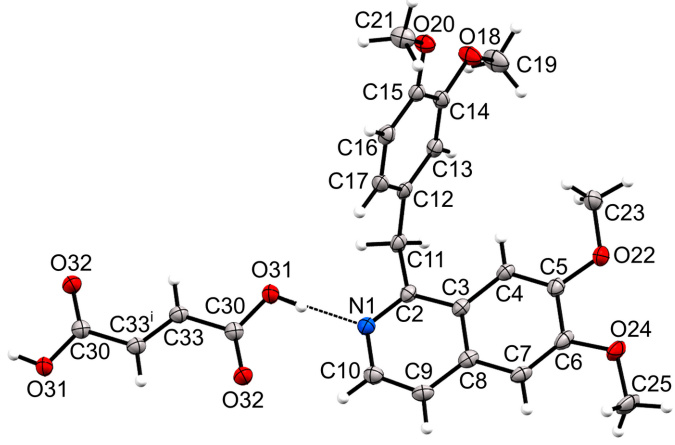


Figure 2
The molecular structure of (II). The hydrogen bond is shown as a dashed line and displacement ellipsoids are drawn at the 50% probability level. [Symmetry code: (i) $-x, -y+1, -z+1$.]

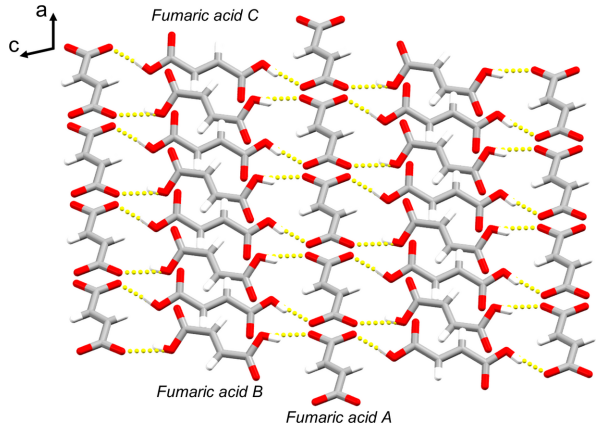


Figure 3
Systematic two-dimensional sheet structure of fumaric acid in (I) viewed along the *ac* plane. Intermolecular O—H···O hydrogen bonds are shown as dashed lines. One of the two disorder components has been omitted for clarity.

shorter than that in neutral or ionic synthons, which indicates an intermediate state between a salt and a co-crystal (Childs *et al.*, 2007; Thipparaboina *et al.*, 2015; Stevens *et al.*, 2020; Tothadi *et al.*, 2021; Kotte *et al.*, 2023). It was thus concluded that this multicomponent crystal, (II), is a salt–co-crystal intermediate.

3. Supramolecular features

The combination of the same two components – papaverine and fumaric acid – led to two different multicomponent crystals each with a different stoichiometric ratio and packing. The fumaric acid molecules in (I) form a systematic two-dimensional sheet structure parallel to the *ac* plane with hydrogen bonds linking fumaric acid molecules *A*, *B*, and *C* (Fig. 3). The space between the fumaric acid sheets is filled with a two-dimensional layer of papaverine molecules hydrogen-bonded to fumaric acid molecules *A*, resulting in (I) having a layered structure (Fig. 4).

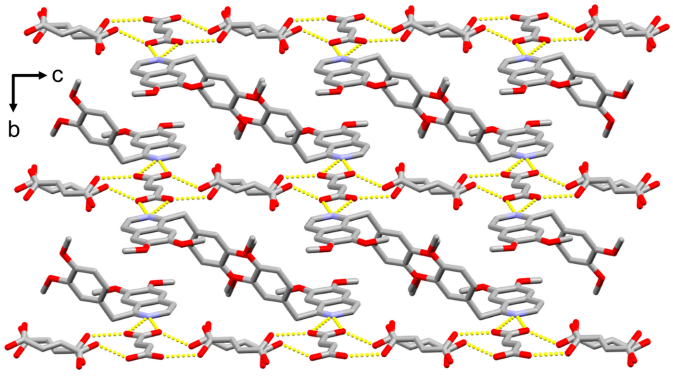


Figure 4
The layered structure of (I) viewed along the *a* axis. Intermolecular O—H···O and N—H···O hydrogen bonds are shown as dashed lines. All hydrogen atoms and one of the two disordered components of the fumaric acid molecules have been omitted for clarity.

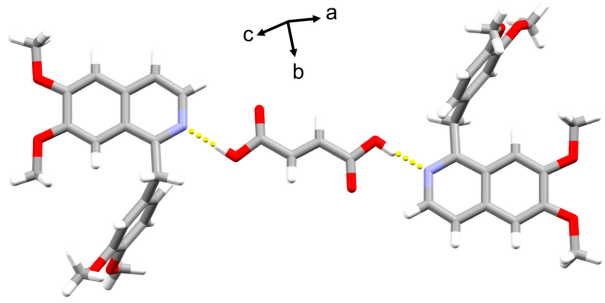


Figure 5
Structural unit in the crystal of (II). Intermolecular O—H···N hydrogen bonds are shown as dashed lines.

Compound (II) exhibits a three-molecule unit structure with hydrogen bonds between two papaverine molecules and one fumaric acid molecule (Fig. 5). The H9···O32 and C9···O32 distances between two of these three-molecule units are 2.2706 (14) and 3.2191 (14) Å, respectively, with a C9—H9···O32 angle of 176.13 (11)° (Fig. 6*a*, Table 2); thus, it was concluded that there is a C—H···O hydrogen bond (Steiner, 1997). A ring structure consisting of two O—H···N hydrogen bonds and two C—H···O hydrogen bonds between two papaverine molecules and two fumaric acid molecules is observed (Fig. 6*a*). As a result, a one-dimensional ribbon structure is formed by the combination of O—H···N and C—H···O hydrogen bonds (Fig. 6*b*). The final crystal structure is formed by the repeated overlapping of these ribbon structures (Fig. 7).

4. Database survey

A survey of the Cambridge Structural Database (WebCSD, v5.44, April 2023; Groom *et al.*, 2016) for structures with

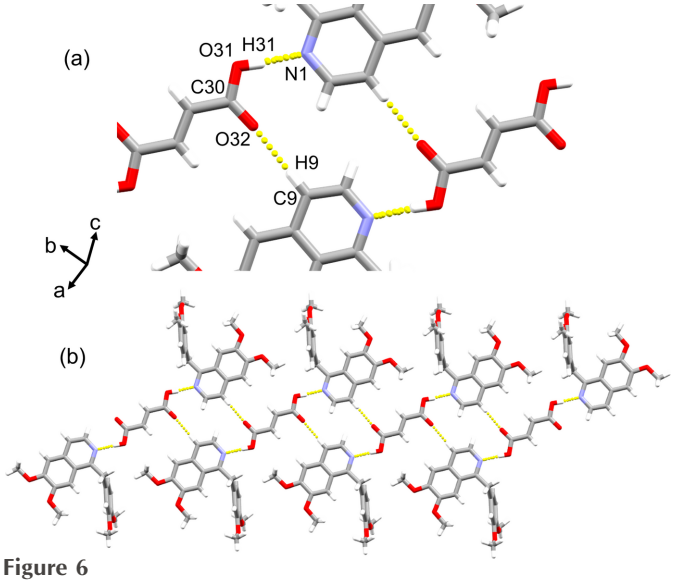


Figure 6
One-dimensional ribbon structure of (II). Intermolecular O—H···N and C—H···O hydrogen bonds are shown as dashed lines. (*a*) Enlarged view of hydrogen-bonded ring. (*b*) Overview of the one-dimensional ribbon structure.

Table 3
Experimental details.

	(I)	(II)
Crystal data		
Chemical formula	$C_{20}H_{22}NO_4{\cdot}1.5C_4H_4O_4$	$C_{20}H_{21}NO_4{\cdot}0.5C_4H_4O_4$
M_r	513.48	397.43
Crystal system, space group	Triclinic, $P\overline{1}$	Monoclinic, $P2_1/n$
Temperature (K)	100	100
a, b, c (Å)	9.5290 (2), 10.5445 (3), 12.6509 (4)	9.05718 (12), 6.71363 (11), 32.8419 (4)
α, β, γ (°)	91.606 (2), 104.980 (2), 97.823 (2)	90, 95.9308 (12), 90
V (Å^3)	1213.87 (6)	1986.31 (5)
Z	2	4
Radiation type	Cu $K\alpha$	Cu $K\alpha$
μ (mm^{-1})	0.92	0.80
Crystal size (mm)	0.17 × 0.08 × 0.03	0.22 × 0.11 × 0.11
Data collection		
Diffractometer	XtaLAB Synergy, Single source at home/near, HyPix3000	XtaLAB Synergy, Single source at home/near, HyPix3000
Absorption correction	Multi-scan (*CrysAlis PRO*; Rigaku OD, 2022)	Multi-scan (*CrysAlis PRO*; Rigaku OD, 2022)
T_{min}, T_{max}	0.862, 1.000	0.908, 1.000
No. of measured, independent and observed reflections	10089, 4366, 3457 [$I > 2\sigma(I)$]	8710, 3589, 3325 [$I \geq 2u(I)$]
R_{int}	0.026	0.018
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0.601	0.601
Refinement		
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.047, 0.133, 1.06	0.033, 0.087, 1.04
No. of reflections	4366	3589
No. of parameters	382	268
No. of restraints	282	0
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.38, −0.39	0.27, −0.21

Computer programs: *CrysAlis PRO* (Rigaku OD, 2022), *SHELXT2018/2* (Sheldrick, 2015*a*), *SHELXL2019/2* (Sheldrick, 2015*b*), *OLEX2.refine* (Bourhis *et al.*, 2015) and *OLEX2* (Dolomanov *et al.*, 2009).

papaverine resulted in four hits. Two crystal structures were free-base, single-component crystals [refcodes MVERIQ (Baggio & Baggio, 1973) and MVERIQ01 (Marek *et al.*, 1997)]. The other two crystals were salts: one was a hydrochloride salt (refcode PAPAVC; Reynolds *et al.*, 1974) and the other was a hydrobromide salt (refcode ZZZGYK; Van Hulle *et al.*, 1953). There were no reports of multi-component crystals of papaverine.

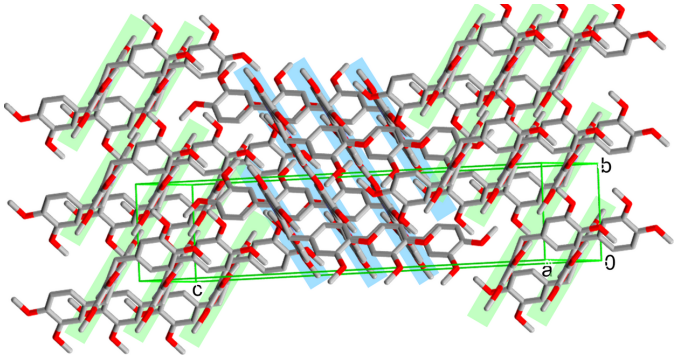


Figure 7
The packing of (II). Each blue and green line represents a one-dimensional ribbon structure. All hydrogen atoms have been removed for clarity.

5. Synthesis and crystallization

Compound (I) was prepared as follows. About 3 mg (0.009 mmol) of papaverine and 2 mg (0.018 mmol) of fumaric acid were dissolved in 0.025 mL of ethanol. The prepared solution was shaken at room temperature at 100 r.p.m. overnight, and clear light colorless, block-shaped crystals were obtained. Compound (II) was prepared as follows. About 20 mg (0.06 mmol) of papaverine and 10 mg (0.09 mmol) of fumaric acid were dissolved in 0.28 mL of a mixture of acetone and water (6:1) with heating at 368K. The prepared solution was shaken at room temperature at 100 r.p.m. overnight, and clear, light, colorless, block-shaped crystals was obtained.

6. Refinement

Crystal data, data collection, and structure refinement details are summarized in Table 3. The N-bound H atom in (I) was positioned geometrically and refined using a riding model with isotropic displacement parameter $U_{iso}(H) = 1.2U_{eq}(N)$. The O-bound H atoms in (I) were located in difference-Fourier maps and refined with O—H = 0.84 Å and with isotropic displacement parameters $U_{iso}(H) = 1.5U_{eq}(O)$. The C-bound H atoms in (I) were positioned geometrically (C—H = 0.95, 0.98, and 0.99 Å for sp^2-hybridized, methyl, and methylene hydrogen atoms, respectively) and refined using a riding model, with isotropic displacement parameters $U_{iso}(H) = 1.5U_{eq}(C)$ for

methyl and U_{iso}(H) = 1.2U_{eq}(C) for all other H atoms. The fumaric acid was disordered over two positions (O39/O40/C41 and C33), for which occupancies were refined, converging to 0.598/0.402 and 0.742/0.258, respectively. Restraints by DFIX were applied for C38/O39/O40, O39/O40, O40/H40, O32/H40, and C38/H40. For compound (II), there were no N-bound H atoms or disorders, and the refinement conditions for O-bound H atoms and C-bound H atoms were the same as those for compound (I).

Acknowledgements

The authors thank Ayano Horikawa (Chugai Pharmaceutical Co., Ltd.) for helpful discussions of the single-crystal structure.

References

Baggio, R. F. & Baggio, S. (1973). *Cryst. Struct. Commun.* **2**, 251–253.
Bharate, S. S. (2021). *Pharm. Res.* **38**, 1307–1326.
Bourhis, L. J., Dolomanov, O. V., Gildea, R. J., Howard, J. A. K. & Puschmann, H. (2015). *Acta Cryst.* A**71**, 59–75.
Chen, J.-M., Wang, Z.-Z., Wu, C.-B., Li, S. & Lu, T.-B. (2012). *CrystEngComm*, **14**, 6221–6229.
Childs, S. L., Stahly, P. & Park, A. (2007). *Mol. Pharm.* **4**, 3, 323–338.
Dolomanov, O. V., Bourhis, L. J., Gildea, R. J., Howard, J. A. K. & Puschmann, H. (2009). *J. Appl. Cryst.* **42**, 339–341.
Groom, C. R., Bruno, I. J., Lightfoot, M. P. & Ward, S. C. (2016). *Acta Cryst.* B**72**, 171–179.
Kang, D., Qiang, G., Du, L. & Du, G. (2018). *Papaverine*. In *Natural Small Molecule Drugs from Plants*. Springer, Singapore.
Kawajiri, T., Kijima, A., Iimuro, A., Ohashi, E., Yamakawa, K., Agura, K., Masuda, K., Kouki, K., Kasamatsu, K., Yanagisawa, S., Nakashima, S., Shibahara, S., Toyota, T., Higuchi, T., Suto, T., Oohara, T., Maki, T., Sahara, N., Fukui, N., Wakamori, H., Ikemoto, H., Murakami, H., Ando, H., Hosoya, M., Sato, M., Suzuki, Y., Nakagawa, Y., Unoh, Y., Hirano, Y., Nagasawa, Y., Goda, S., Ohara, T. & Tsuritani, T. (2023). *ACS Cent. Sci.* **9**, 836–843
Kotte, L., Pendota, V., Sreedhar, B. & Nanubolu, J. B. (2023). *CrystEngComm*, **25**, 2662–2678.
Marek, J., Dostal, J. & Slavik, J. (1997). *Z. Kristallogr. Cryst. Mater.* **211**, 649–650.
Reynolds, C. D., Palmer, R. A. & Gorinsky, B. (1974). *J. Cryst. Mol. Struct.* **4**, 213–225.
Rigaku OD (2022). *CrysAlis PRO*. Rigaku Oxford Diffraction, Yarnton, England.
Sheldrick, G. M. (2015*a*). *Acta Cryst.* A**71**, 3–8.
Sheldrick, G. M. (2015*b*). *Acta Cryst.* C**71**, 3–8.
Steiner, T. (1997). *Chem. Commun.* pp. 727–734.
Stevens, J. S., Coultas, S., Jaye, C., Fischer, D. A. & Schroeder, S. L. M. (2020). *Phys. Chem. Chem. Phys.* **22**, 4916–4923.
Thipparaboina, R., Kumar, D., Mittapalli, S., Balasubramanian, S., Nangia, A. & Shastri, N. R. (2015). *Cryst. Growth Des.* **15**, 12, 5816–5826.
Tothadi, S., Shaikh, T. R., Gupta, S., Dandela, R., Vinod, C. P. & Nangia, A. K. (2021). *Cryst. Growth Des.* **21**, 2, 735–747.
Van Hulle, A., Amelinckx, S. & Dekeyser, W. (1953). *Acta Cryst.* **6**, 664–665.

supporting information

Acta Cryst. (2024). E**80**, 1146-1150 [https://doi.org/10.1107/S2056989024009794]

Crystal structures of two different multi-component crystals consisting of 1-(3,4-dimethoxybenzyl)-6,7-dimethoxyisoquinoline and fumaric acid

Hiroki Shibata, Aya Sakon, Noriyuki Takata and Hiroshi Takiyama

Computing details

1-(3,4-Dimethoxybenzyl)-6,7-dimethoxyisoquinoline–fumaric acid (2/1) (II)

Crystal data

$C_{20}H_{21}NO_4 \cdot 0.5C_4H_4O_4$
$M_r = 397.43$
Monoclinic, $P2_1/n$
$a = 9.05718\ (12)$ Å
$b = 6.71363\ (11)$ Å
$c = 32.8419\ (4)$ Å
$\beta = 95.9308\ (12)°$
$V = 1986.31\ (5)$ Å^3
$Z = 4$
$F(000) = 843.079$
$D_x = 1.329$ Mg m^{-3}
Cu $K\alpha$ radiation, $\lambda = 1.54184$ Å
Cell parameters from 6957 reflections
$\theta = 2.7–67.9°$
$\mu = 0.80$ mm^{-1}
$T = 100$ K
Block, clear light colourless
0.22 × 0.11 × 0.11 mm

Data collection

XtaLAB Synergy, Single source at home/near, HyPix3000 diffractometer
Radiation source: micro-focus sealed X-ray tube, PhotonJet (Cu) X-ray Source
Mirror monochromator
Detector resolution: 10.0000 pixels mm^{-1}
ω scans
Absorption correction: multi-scan (CrysAlisPro; Rigaku OD, 2022)
$T_{min} = 0.908$, $T_{max} = 1.000$
8710 measured reflections
3589 independent reflections
3325 reflections with $I \geq 2u(I)$
$R_{int} = 0.018$
$\theta_{max} = 68.0°$, $\theta_{min} = 2.7°$
$h = -10 \rightarrow 5$
$k = -8 \rightarrow 8$
$l = -39 \rightarrow 39$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.033$
$wR(F^2) = 0.087$
$S = 1.04$
3589 reflections
268 parameters
0 restraints
37 constraints
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0429P)^2 + 0.6045P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = -0.0003$
$\Delta\rho_{max} = 0.27$ e Å^{-3}
$\Delta\rho_{min} = -0.21$ e Å^{-3}
Extinction correction: *SHELXL2019/2* (Sheldrick, 2015b), $Fc^* = kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.0012 (2)

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
N1	0.51693 (10)	0.60177 (14)	0.44622 (3)	0.0210 (2)
C2	0.60617 (12)	0.51334 (17)	0.42229 (3)	0.0187 (2)
C3	0.74048 (11)	0.60359 (17)	0.41307 (3)	0.0182 (2)
C4	0.83390 (12)	0.51426 (17)	0.38613 (3)	0.0197 (2)
H4	0.80587 (12)	0.39140 (17)	0.37322 (3)	0.0237 (3)*
C5	0.96396 (12)	0.60367 (18)	0.37863 (3)	0.0218 (2)
C6	1.00943 (13)	0.78635 (18)	0.39912 (3)	0.0238 (3)
C7	0.92008 (13)	0.87524 (17)	0.42489 (3)	0.0229 (3)
H7	0.94998 (13)	0.99708 (17)	0.43796 (3)	0.0274 (3)*
C8	0.78282 (12)	0.78679 (17)	0.43229 (3)	0.0200 (2)
C9	0.68699 (13)	0.87280 (17)	0.45879 (3)	0.0227 (2)
H9	0.71313 (13)	0.99387 (17)	0.47268 (3)	0.0272 (3)*
C10	0.55693 (13)	0.77991 (18)	0.46414 (3)	0.0233 (3)
H10	0.49118 (13)	0.84156 (18)	0.48104 (3)	0.0279 (3)*
C11	0.56339 (12)	0.30741 (17)	0.40725 (3)	0.0206 (2)
H11a	0.47821 (12)	0.26165 (17)	0.42142 (3)	0.0247 (3)*
H11b	0.64743 (12)	0.21623 (17)	0.41512 (3)	0.0247 (3)*
C12	0.52185 (11)	0.29044 (16)	0.36140 (3)	0.0192 (2)
C13	0.58166 (12)	0.13608 (17)	0.33954 (3)	0.0205 (2)
H13	0.64718 (12)	0.04275 (17)	0.35364 (3)	0.0246 (3)*
C14	0.54649 (12)	0.11766 (17)	0.29756 (3)	0.0208 (2)
C15	0.44833 (11)	0.25584 (17)	0.27672 (3)	0.0200 (2)
C16	0.38820 (12)	0.40628 (17)	0.29850 (4)	0.0223 (2)
H16	0.32136 (12)	0.49876 (17)	0.28463 (4)	0.0268 (3)*
C17	0.42478 (12)	0.42374 (17)	0.34077 (4)	0.0219 (2)
H17	0.38266 (12)	0.52785 (17)	0.35539 (4)	0.0262 (3)*
O18	0.60006 (10)	−0.02676 (13)	0.27362 (3)	0.0286 (2)
C19	0.70127 (16)	−0.1679 (2)	0.29353 (4)	0.0363 (3)
H19a	0.7335 (9)	−0.2609 (10)	0.27322 (6)	0.0545 (5)*
H19b	0.7878 (6)	−0.0977 (3)	0.3070 (3)	0.0545 (5)*
H19c	0.6519 (4)	−0.2418 (11)	0.3140 (2)	0.0545 (5)*
O20	0.41893 (9)	0.22626 (12)	0.23544 (2)	0.0241 (2)
C21	0.32565 (14)	0.37026 (19)	0.21353 (4)	0.0291 (3)
H21a	0.3150 (9)	0.3372 (8)	0.18431 (5)	0.0436 (4)*
H21b	0.2278 (4)	0.3696 (10)	0.2238 (2)	0.0436 (4)*
H21c	0.3702 (6)	0.5028 (3)	0.2175 (2)	0.0436 (4)*
O22	1.05851 (9)	0.53419 (14)	0.35250 (3)	0.0282 (2)
C23	1.00672 (13)	0.37103 (19)	0.32693 (4)	0.0289 (3)
H23a	1.0801 (5)	0.3403 (9)	0.3079 (2)	0.0433 (4)*
H23b	0.9924 (10)	0.2541 (4)	0.34395 (4)	0.0433 (4)*
H23c	0.9122 (5)	0.4069 (5)	0.3114 (2)	0.0433 (4)*
O24	1.14269 (9)	0.85526 (14)	0.39014 (3)	0.0324 (2)
C25	1.20004 (16)	1.0296 (2)	0.41170 (4)	0.0373 (3)
H25a	1.2970 (6)	1.0637 (10)	0.4028 (3)	0.0559 (5)*
H25b	1.1312 (6)	1.1410 (5)	0.4058 (3)	0.0559 (5)*

H25c	1.2110 (12)	1.0031 (6)	0.44120 (5)	0.0559 (5)*
C30	0.18953 (12)	0.55150 (17)	0.48065 (3)	0.0206 (2)
O31	0.26149 (9)	0.45088 (13)	0.45496 (3)	0.0256 (2)
H31	0.3443 (7)	0.5047 (14)	0.4531 (4)	0.0384 (3)*
O32	0.23373 (9)	0.70574 (13)	0.49758 (3)	0.0272 (2)
C33	0.04511 (12)	0.45913 (17)	0.48787 (3)	0.0213 (2)
H33	0.01702 (12)	0.33727 (17)	0.47454 (3)	0.0256 (3)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0193 (4)	0.0212 (5)	0.0225 (5)	−0.0011 (4)	0.0023 (4)	−0.0005 (4)
C2	0.0174 (5)	0.0194 (6)	0.0189 (5)	−0.0011 (4)	−0.0002 (4)	0.0019 (4)
C3	0.0178 (5)	0.0175 (5)	0.0188 (5)	−0.0022 (4)	−0.0011 (4)	0.0029 (4)
C4	0.0191 (5)	0.0184 (5)	0.0213 (5)	−0.0041 (4)	0.0002 (4)	0.0003 (4)
C5	0.0196 (5)	0.0252 (6)	0.0207 (5)	−0.0036 (5)	0.0024 (4)	0.0016 (5)
C6	0.0226 (6)	0.0275 (6)	0.0209 (5)	−0.0114 (5)	0.0002 (4)	0.0043 (5)
C7	0.0271 (6)	0.0196 (6)	0.0209 (5)	−0.0084 (5)	−0.0022 (4)	0.0012 (4)
C8	0.0227 (5)	0.0175 (6)	0.0189 (5)	−0.0024 (4)	−0.0025 (4)	0.0035 (4)
C9	0.0280 (6)	0.0178 (6)	0.0214 (5)	−0.0016 (5)	−0.0012 (4)	−0.0014 (4)
C10	0.0251 (6)	0.0211 (6)	0.0236 (6)	0.0010 (5)	0.0024 (4)	−0.0019 (5)
C11	0.0183 (5)	0.0190 (6)	0.0250 (6)	−0.0048 (4)	0.0041 (4)	0.0004 (4)
C12	0.0144 (5)	0.0185 (5)	0.0251 (6)	−0.0061 (4)	0.0034 (4)	−0.0014 (4)
C13	0.0163 (5)	0.0178 (5)	0.0272 (6)	−0.0009 (4)	0.0014 (4)	0.0009 (4)
C14	0.0180 (5)	0.0177 (5)	0.0271 (6)	0.0001 (4)	0.0045 (4)	−0.0026 (4)
C15	0.0172 (5)	0.0194 (5)	0.0234 (5)	−0.0031 (4)	0.0022 (4)	−0.0007 (4)
C16	0.0180 (5)	0.0195 (6)	0.0290 (6)	0.0011 (4)	0.0006 (4)	0.0001 (5)
C17	0.0185 (5)	0.0192 (6)	0.0282 (6)	−0.0003 (4)	0.0040 (4)	−0.0046 (5)
O18	0.0330 (4)	0.0255 (4)	0.0267 (4)	0.0120 (4)	0.0012 (3)	−0.0044 (3)
C19	0.0401 (7)	0.0313 (7)	0.0368 (7)	0.0189 (6)	0.0001 (6)	−0.0051 (6)
O20	0.0265 (4)	0.0225 (4)	0.0228 (4)	0.0041 (3)	0.0006 (3)	−0.0012 (3)
C21	0.0370 (7)	0.0237 (6)	0.0259 (6)	0.0057 (5)	0.0000 (5)	0.0030 (5)
O22	0.0229 (4)	0.0333 (5)	0.0300 (4)	−0.0099 (4)	0.0098 (3)	−0.0059 (4)
C23	0.0282 (6)	0.0286 (7)	0.0314 (6)	−0.0063 (5)	0.0111 (5)	−0.0056 (5)
O24	0.0281 (4)	0.0398 (5)	0.0303 (4)	−0.0218 (4)	0.0071 (3)	−0.0050 (4)
C25	0.0372 (7)	0.0431 (8)	0.0313 (6)	−0.0279 (6)	0.0021 (5)	−0.0028 (6)
C30	0.0217 (5)	0.0200 (6)	0.0200 (5)	−0.0001 (4)	0.0019 (4)	0.0010 (4)
O31	0.0217 (4)	0.0257 (4)	0.0307 (4)	−0.0044 (3)	0.0092 (3)	−0.0064 (3)
O32	0.0252 (4)	0.0246 (5)	0.0326 (4)	−0.0063 (3)	0.0071 (3)	−0.0078 (4)
C33	0.0223 (5)	0.0197 (6)	0.0218 (5)	−0.0019 (4)	0.0014 (4)	−0.0011 (4)

Geometric parameters (Å, º)

N1—C2	1.3245 (14)	C15—C16	1.3817 (16)
N1—C10	1.3652 (15)	C15—O20	1.3688 (13)
C2—C3	1.4195 (15)	C16—H16	0.9500
C2—C11	1.5053 (15)	C16—C17	1.3984 (16)
C3—C4	1.4187 (16)	C17—H17	0.9500

C3—C8	1.4172 (16)	O18—C19	1.4288 (15)
C4—H4	0.9500	C19—H19a	0.9800
C4—C5	1.3670 (15)	C19—H19b	0.9800
C5—C6	1.4386 (17)	C19—H19c	0.9800
C5—O22	1.3561 (14)	O20—C21	1.4285 (14)
C6—C7	1.3670 (17)	C21—H21a	0.9800
C6—O24	1.3533 (14)	C21—H21b	0.9800
C7—H7	0.9500	C21—H21c	0.9800
C7—C8	1.4211 (16)	O22—C23	1.4296 (15)
C8—C9	1.4145 (16)	C23—H23a	0.9800
C9—H9	0.9500	C23—H23b	0.9800
C9—C10	1.3602 (17)	C23—H23c	0.9800
C10—H10	0.9500	O24—C25	1.4372 (15)
C11—H11a	0.9900	C25—H25a	0.9800
C11—H11b	0.9900	C25—H25b	0.9800
C11—C12	1.5183 (15)	C25—H25c	0.9800
C12—C13	1.4011 (16)	C30—O31	1.3064 (14)
C12—C17	1.3819 (16)	C30—O32	1.2230 (14)
C13—H13	0.9500	C30—C33	1.4884 (16)
C13—C14	1.3880 (16)	O31—H31	0.8400
C14—C15	1.4120 (16)	C33—C33^{i}	1.319 (2)
C14—O18	1.3684 (14)	C33—H33	0.9500

C10—N1—C2	119.83 (10)	C16—C15—C14	119.43 (10)
C3—C2—N1	121.62 (10)	O20—C15—C14	115.67 (10)
C11—C2—N1	117.02 (9)	O20—C15—C16	124.90 (10)
C11—C2—C3	121.27 (10)	H16—C16—C15	119.68 (7)
C4—C3—C2	122.15 (10)	C17—C16—C15	120.64 (10)
C8—C3—C2	118.28 (10)	C17—C16—H16	119.68 (7)
C8—C3—C4	119.55 (10)	C16—C17—C12	120.38 (10)
H4—C4—C3	119.75 (6)	H17—C17—C12	119.81 (7)
C5—C4—C3	120.49 (10)	H17—C17—C16	119.81 (7)
C5—C4—H4	119.75 (7)	C19—O18—C14	117.12 (9)
C6—C5—C4	120.02 (10)	H19a—C19—O18	109.5
O22—C5—C4	125.12 (11)	H19b—C19—O18	109.5
O22—C5—C6	114.86 (10)	H19b—C19—H19a	109.5
C7—C6—C5	120.18 (10)	H19c—C19—O18	109.5
O24—C6—C5	114.08 (10)	H19c—C19—H19a	109.5
O24—C6—C7	125.74 (11)	H19c—C19—H19b	109.5
H7—C7—C6	119.75 (7)	C21—O20—C15	116.43 (9)
C8—C7—C6	120.51 (10)	H21a—C21—O20	109.5
C8—C7—H7	119.75 (7)	H21b—C21—O20	109.5
C7—C8—C3	119.20 (10)	H21b—C21—H21a	109.5
C9—C8—C3	118.26 (10)	H21c—C21—O20	109.5
C9—C8—C7	122.54 (10)	H21c—C21—H21a	109.5
H9—C9—C8	120.43 (6)	H21c—C21—H21b	109.5
C10—C9—C8	119.14 (10)	C23—O22—C5	116.42 (9)
C10—C9—H9	120.43 (7)	H23a—C23—O22	109.5

C9—C10—N1	122.73 (11)	H23b—C23—O22	109.5
H10—C10—N1	118.63 (6)	H23b—C23—H23a	109.5
H10—C10—C9	118.63 (7)	H23c—C23—O22	109.5
H11a—C11—C2	108.51 (6)	H23c—C23—H23a	109.5
H11b—C11—C2	108.51 (6)	H23c—C23—H23b	109.5
H11b—C11—H11a	107.5	C25—O24—C6	117.14 (10)
C12—C11—C2	115.05 (9)	H25a—C25—O24	109.5
C12—C11—H11a	108.51 (5)	H25b—C25—O24	109.5
C12—C11—H11b	108.51 (6)	H25b—C25—H25a	109.5
C13—C12—C11	119.63 (10)	H25c—C25—O24	109.5
C17—C12—C11	121.16 (10)	H25c—C25—H25a	109.5
C17—C12—C13	119.20 (10)	H25c—C25—H25b	109.5
H13—C13—C12	119.55 (6)	O32—C30—O31	124.73 (10)
C14—C13—C12	120.90 (10)	C33—C30—O31	113.12 (10)
C14—C13—H13	119.55 (7)	C33—C30—O32	122.15 (10)
C15—C14—C13	119.43 (10)	H31—O31—C30	109.5
O18—C14—C13	125.11 (10)	C33^{i}—C33—C30	122.17 (13)
O18—C14—C15	115.46 (10)	H33—C33—C30	118.91 (6)

N1—C2—C3—C4	−177.32 (10)	C5—C6—C7—C8	1.10 (13)
N1—C2—C3—C8	4.06 (12)	C5—C6—O24—C25	−175.75 (11)
N1—C2—C11—C12	113.81 (10)	C6—C7—C8—C9	179.76 (11)
N1—C10—C9—C8	2.72 (13)	C7—C8—C9—C10	179.60 (11)
C2—C3—C4—C5	−178.66 (11)	C11—C12—C13—C14	−179.55 (10)
C2—C3—C8—C7	177.22 (10)	C11—C12—C17—C16	179.76 (10)
C2—C3—C8—C9	−1.70 (12)	C12—C13—C14—C15	−0.40 (12)
C2—C11—C12—C13	133.10 (9)	C12—C13—C14—O18	179.50 (10)
C2—C11—C12—C17	−47.48 (11)	C12—C17—C16—C15	0.01 (13)
C3—C4—C5—C6	2.05 (12)	C13—C14—C15—C16	−0.41 (12)
C3—C4—C5—O22	−177.78 (10)	C13—C14—C15—O20	−179.63 (10)
C3—C8—C7—C6	0.89 (12)	C13—C14—O18—C19	−0.69 (14)
C3—C8—C9—C10	−1.52 (12)	C14—C15—C16—C17	0.61 (12)
C4—C5—C6—C7	−2.60 (13)	C14—C15—O20—C21	−177.02 (10)
C4—C5—C6—O24	177.69 (11)	C30—C33—C33^{i}—C30^{i}	180.00 (14)
C4—C5—O22—C23	9.21 (14)		

Symmetry code: (i) −*x*, −*y*+1, −*z*+1.

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O31—H31···N1	0.84 (1)	1.73 (1)	2.5687 (12)	175 (1)
C9—H9···O32^{ii}	0.95 (1)	2.27 (1)	3.2191 (14)	176 (1)

Symmetry code: (ii) −*x*+1, −*y*+2, −*z*+1.

1-(3,4-Dimethoxybenzyl)-6,7-dimethoxyisoquinoline–fumaric acid (2/3) (I)

Crystal data

$C_{20}H_{22}NO_4 \cdot 1.5C_4H_4O_4$
$M_r = 513.48$
Triclinic, $P\overline{1}$
$a = 9.5290$ (2) Å
$b = 10.5445$ (3) Å
$c = 12.6509$ (4) Å
$\alpha = 91.606$ (2)°
$\beta = 104.980$ (2)°
$\gamma = 97.823$ (2)°
$V = 1213.87$ (6) Å^3
$Z = 2$
$F(000) = 540$
$D_x = 1.405$ Mg m^{-3}
Cu $K\alpha$ radiation, $\lambda = 1.54184$ Å
Cell parameters from 6061 reflections
$\theta = 3.6$–$68.1°$
$\mu = 0.92$ mm^{-1}
$T = 100$ K
Block, clear light colourless
0.17 × 0.08 × 0.03 mm

Data collection

XtaLAB Synergy, Single source at home/near, HyPix3000 diffractometer
Radiation source: micro-focus sealed X-ray tube, PhotonJet (Cu) X-ray Source
Mirror monochromator
Detector resolution: 10.0000 pixels mm^{-1}
ω scans
Absorption correction: multi-scan (CrysAlisPro; Rigaku OD, 2022)
$T_{min} = 0.862$, $T_{max} = 1.000$
10089 measured reflections
4366 independent reflections
3457 reflections with $I > 2\sigma(I)$
$R_{int} = 0.026$
$\theta_{max} = 68.0°$, $\theta_{min} = 3.6°$
$h = -11 \rightarrow 5$
$k = -12 \rightarrow 12$
$l = -15 \rightarrow 15$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.047$
$wR(F^2) = 0.133$
$S = 1.06$
4366 reflections
382 parameters
282 restraints
Primary atom site location: structure-invariant direct methods
Hydrogen site location: mixed
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0609P)^2 + 0.410P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.38$ e Å^{-3}
$\Delta\rho_{min} = -0.39$ e Å^{-3}
Extinction correction: *SHELXL2019/2* (Sheldrick, 2015b), $Fc^* = kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.0009 (3)

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}	Occ. (<1)
N1	0.46197 (17)	0.81758 (17)	0.51609 (18)	0.0444 (5)	
H1	0.543685	0.850236	0.500466	0.053*	
C2	0.3393 (2)	0.79572 (18)	0.43509 (19)	0.0359 (5)	
C3	0.20717 (19)	0.74256 (17)	0.45885 (17)	0.0303 (4)	
C4	0.07358 (18)	0.71542 (17)	0.37492 (16)	0.0286 (4)	
H4	0.073022	0.730035	0.301067	0.034*	

C5	−0.05396 (18)	0.66853 (17)	0.39956 (16)	0.0289 (4)
C6	−0.05444 (19)	0.64893 (17)	0.51115 (17)	0.0301 (4)
C7	0.0738 (2)	0.67300 (17)	0.59334 (17)	0.0326 (4)
H7	0.072747	0.659166	0.667034	0.039*
C8	0.2077 (2)	0.71842 (17)	0.56852 (17)	0.0320 (4)
C9	0.3442 (2)	0.7438 (2)	0.6496 (2)	0.0430 (5)
H9	0.349081	0.726778	0.723680	0.052*
C10	0.4681 (2)	0.7924 (2)	0.6211 (2)	0.0492 (6)
H10	0.559426	0.808756	0.675412	0.059*
C11	0.3489 (2)	0.83103 (18)	0.3232 (2)	0.0404 (5)
H11A	0.440287	0.891577	0.330194	0.049*
H11B	0.264971	0.875706	0.289528	0.049*
C12	0.3477 (2)	0.71580 (18)	0.24786 (19)	0.0356 (5)
C13	0.2463 (2)	0.69676 (18)	0.14486 (19)	0.0359 (5)
H13	0.176960	0.754304	0.123955	0.043*
C14	0.2456 (2)	0.59499 (19)	0.07283 (18)	0.0352 (4)
C15	0.3481 (2)	0.50903 (18)	0.10481 (17)	0.0338 (4)
C16	0.4475 (2)	0.52812 (18)	0.20657 (17)	0.0342 (4)
H16	0.515980	0.470031	0.228377	0.041*
C17	0.4487 (2)	0.63203 (18)	0.27815 (18)	0.0343 (4)
H17	0.518893	0.645061	0.347593	0.041*
O18	0.15271 (16)	0.56999 (14)	−0.02976 (13)	0.0416 (4)
C19	0.0454 (2)	0.6537 (2)	−0.0642 (2)	0.0451 (5)
H19A	−0.018009	0.622919	−0.137013	0.068*
H19B	0.095157	0.740628	−0.067495	0.068*
H19C	−0.014298	0.654835	−0.011816	0.068*
O20	0.33975 (16)	0.41301 (14)	0.02746 (12)	0.0415 (4)
C21	0.4403 (3)	0.3231 (2)	0.05620 (19)	0.0458 (5)
H21A	0.429616	0.263692	−0.007301	0.069*
H21B	0.419471	0.274827	0.116846	0.069*
H21C	0.540978	0.369063	0.078816	0.069*
O22	−0.18676 (13)	0.63998 (14)	0.32630 (12)	0.0370 (3)
C23	−0.1929 (2)	0.6669 (3)	0.21502 (19)	0.0514 (6)
H23A	−0.295060	0.649292	0.170510	0.077*
H23B	−0.133712	0.612563	0.186378	0.077*
H23C	−0.154234	0.757365	0.212015	0.077*
O24	−0.18929 (14)	0.60799 (13)	0.52392 (12)	0.0375 (3)
C25	−0.2027 (3)	0.6004 (2)	0.63391 (19)	0.0451 (5)
H25A	−0.305854	0.573898	0.632334	0.068*
H25B	−0.167756	0.684678	0.673616	0.068*
H25C	−0.143486	0.537523	0.670996	0.068*
C34	0.6558 (2)	1.03159 (19)	0.13490 (18)	0.0369 (5)
O35	0.60430 (18)	0.93880 (15)	0.18930 (13)	0.0484 (4)
H35	0.654420	0.946279	0.254974	0.073*
O36	0.76487 (17)	1.10891 (15)	0.17335 (14)	0.0477 (4)
C37	0.5660 (2)	1.03429 (18)	0.02071 (18)	0.0368 (5)
H37	0.605453	1.088822	−0.026367	0.044*
C38	0.9160 (2)	0.9597 (2)	0.8450 (2)	0.0504 (6)

O39A	0.9425 (5)	1.0085 (3)	0.7594 (3)	0.0410 (9)	0.598 (9)
H39A	0.883696	0.969476	0.703076	0.062*	0.598 (9)
O39B	0.9637 (9)	1.0502 (9)	0.7980 (9)	0.091 (3)	0.402 (9)
O40A	0.8223 (6)	0.8669 (5)	0.8449 (3)	0.0554 (11)	0.598 (9)
O40B	0.8172 (9)	0.8612 (7)	0.8033 (9)	0.095 (3)	0.402 (9)
H40B	0.804 (10)	0.868 (7)	0.7354 (12)	0.142*	0.402 (9)
C41A	1.0105 (5)	1.0188 (5)	0.9512 (4)	0.0314 (11)	0.598 (9)
H41A	1.088580	1.085283	0.951450	0.038*	0.598 (9)
C41B	0.9522 (9)	0.9608 (9)	0.9704 (8)	0.047 (2)	0.402 (9)
H41B	0.898144	0.898230	1.002913	0.057*	0.402 (9)
C30	0.7944 (2)	0.94153 (17)	0.48749 (18)	0.0334 (4)	
O31	0.69127 (18)	0.92626 (15)	0.40213 (14)	0.0491 (4)	
O32	0.77542 (17)	0.91662 (14)	0.57896 (13)	0.0448 (4)	
C33A	0.9361 (4)	0.9954 (2)	0.4628 (4)	0.0278 (11)	0.742 (11)
H33A	0.933667	1.023721	0.391822	0.033*	0.742 (11)
C33B	0.9632 (11)	0.9786 (7)	0.5352 (10)	0.030 (3)	0.258 (11)
H33B	1.010435	0.971108	0.610235	0.036*	0.258 (11)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0222 (8)	0.0367 (9)	0.0710 (14)	0.0039 (6)	0.0085 (8)	−0.0155 (9)
C2	0.0237 (9)	0.0261 (9)	0.0583 (13)	0.0035 (7)	0.0131 (9)	−0.0100 (8)
C3	0.0228 (8)	0.0239 (8)	0.0446 (12)	0.0056 (6)	0.0094 (8)	−0.0053 (8)
C4	0.0246 (8)	0.0280 (9)	0.0347 (10)	0.0044 (7)	0.0105 (8)	−0.0023 (7)
C5	0.0223 (8)	0.0281 (9)	0.0354 (10)	0.0033 (7)	0.0072 (7)	−0.0049 (7)
C6	0.0272 (9)	0.0252 (9)	0.0406 (11)	0.0032 (7)	0.0145 (8)	−0.0021 (8)
C7	0.0372 (10)	0.0276 (9)	0.0349 (11)	0.0093 (7)	0.0107 (8)	0.0002 (8)
C8	0.0286 (9)	0.0263 (9)	0.0402 (11)	0.0097 (7)	0.0052 (8)	−0.0047 (8)
C9	0.0397 (11)	0.0355 (11)	0.0476 (13)	0.0164 (8)	−0.0039 (9)	−0.0101 (9)
C10	0.0257 (10)	0.0407 (12)	0.0709 (17)	0.0117 (8)	−0.0066 (10)	−0.0190 (11)
C11	0.0317 (10)	0.0281 (9)	0.0681 (15)	−0.0007 (7)	0.0282 (10)	−0.0027 (9)
C12	0.0284 (9)	0.0271 (9)	0.0590 (14)	0.0022 (7)	0.0260 (9)	0.0019 (9)
C13	0.0296 (9)	0.0301 (9)	0.0567 (13)	0.0094 (7)	0.0236 (9)	0.0100 (9)
C14	0.0332 (10)	0.0347 (10)	0.0450 (12)	0.0082 (8)	0.0211 (9)	0.0106 (8)
C15	0.0362 (10)	0.0319 (9)	0.0418 (12)	0.0106 (8)	0.0218 (9)	0.0071 (8)
C16	0.0334 (9)	0.0323 (10)	0.0445 (12)	0.0113 (7)	0.0199 (9)	0.0060 (8)
C17	0.0270 (9)	0.0332 (10)	0.0475 (12)	0.0029 (7)	0.0197 (8)	0.0002 (8)
O18	0.0433 (8)	0.0432 (8)	0.0438 (9)	0.0172 (6)	0.0150 (7)	0.0102 (7)
C19	0.0401 (11)	0.0467 (12)	0.0550 (14)	0.0166 (9)	0.0175 (10)	0.0168 (11)
O20	0.0536 (8)	0.0386 (8)	0.0389 (8)	0.0213 (7)	0.0164 (7)	0.0036 (6)
C21	0.0624 (14)	0.0410 (12)	0.0420 (13)	0.0261 (10)	0.0182 (11)	0.0036 (10)
O22	0.0212 (6)	0.0521 (8)	0.0353 (8)	0.0007 (5)	0.0062 (5)	−0.0040 (6)
C23	0.0283 (10)	0.0872 (18)	0.0347 (12)	0.0023 (10)	0.0051 (9)	0.0011 (12)
O24	0.0320 (7)	0.0389 (7)	0.0457 (9)	−0.0017 (5)	0.0213 (6)	−0.0004 (6)
C25	0.0530 (13)	0.0430 (12)	0.0507 (14)	0.0094 (10)	0.0322 (11)	0.0067 (10)
C34	0.0422 (11)	0.0301 (10)	0.0452 (12)	0.0068 (8)	0.0227 (9)	0.0024 (8)
O35	0.0550 (9)	0.0476 (9)	0.0401 (9)	−0.0056 (7)	0.0147 (7)	0.0075 (7)

O36	0.0445 (8)	0.0464 (9)	0.0528 (10)	−0.0001 (7)	0.0169 (7)	0.0068 (7)
C37	0.0462 (11)	0.0294 (9)	0.0420 (12)	0.0073 (8)	0.0237 (9)	0.0034 (8)
C38	0.0472 (13)	0.0539 (14)	0.0506 (15)	0.0289 (11)	0.0036 (11)	−0.0042 (11)
O39A	0.0466 (17)	0.0416 (16)	0.0310 (18)	0.0077 (12)	0.0045 (15)	−0.0136 (12)
O39B	0.069 (4)	0.150 (6)	0.068 (6)	0.054 (5)	0.020 (4)	0.054 (5)
O40A	0.079 (3)	0.075 (3)	0.0154 (18)	0.0210 (18)	0.0145 (19)	0.0043 (17)
O40B	0.086 (4)	0.082 (4)	0.082 (6)	0.042 (3)	−0.048 (4)	−0.058 (4)
C41A	0.034 (2)	0.035 (2)	0.031 (3)	0.0118 (16)	0.0154 (18)	0.0083 (17)
C41B	0.043 (4)	0.050 (4)	0.048 (5)	0.021 (3)	0.002 (3)	0.005 (3)
C30	0.0262 (9)	0.0246 (9)	0.0509 (13)	0.0034 (7)	0.0140 (9)	−0.0030 (8)
O31	0.0561 (9)	0.0458 (9)	0.0434 (9)	0.0058 (7)	0.0104 (8)	0.0035 (7)
O32	0.0540 (9)	0.0415 (8)	0.0426 (9)	0.0160 (7)	0.0147 (7)	0.0036 (7)
C33A	0.0264 (19)	0.0261 (13)	0.032 (2)	0.0037 (10)	0.0103 (15)	0.0011 (11)
C33B	0.033 (5)	0.026 (4)	0.030 (7)	0.006 (3)	0.003 (3)	0.001 (3)

Geometric parameters (Å, º)

N1—H1	0.8800	C21—H21A	0.9800
N1—C2	1.328 (3)	C21—H21B	0.9800
N1—C10	1.350 (3)	C21—H21C	0.9800
C2—C3	1.415 (3)	O22—C23	1.432 (3)
C2—C11	1.496 (3)	C23—H23A	0.9800
C3—C4	1.419 (3)	C23—H23B	0.9800
C3—C8	1.416 (3)	C23—H23C	0.9800
C4—H4	0.9500	O24—C25	1.433 (3)
C4—C5	1.364 (3)	C25—H25A	0.9800
C5—C6	1.434 (3)	C25—H25B	0.9800
C5—O22	1.351 (2)	C25—H25C	0.9800
C6—C7	1.372 (3)	C34—O35	1.324 (2)
C6—O24	1.351 (2)	C34—O36	1.211 (3)
C7—H7	0.9500	C34—C37	1.480 (3)
C7—C8	1.416 (3)	O35—H35	0.8400
C8—C9	1.420 (3)	C37—C37^{i}	1.331 (4)
C9—H9	0.9500	C37—H37	0.9500
C9—C10	1.361 (4)	C38—O39A	1.280 (4)
C10—H10	0.9500	C38—O39B	1.235 (5)
C11—H11A	0.9900	C38—O40A	1.231 (4)
C11—H11B	0.9900	C38—O40B	1.300 (5)
C11—C12	1.520 (3)	C38—C41A	1.476 (6)
C12—C13	1.398 (3)	C38—C41B	1.533 (10)
C12—C17	1.383 (3)	O39A—H39A	0.8400
C13—H13	0.9500	O40B—H40B	0.843 (5)
C13—C14	1.386 (3)	C41A—C41A^{ii}	1.362 (9)
C14—C15	1.413 (3)	C41A—H41A	0.9500
C14—O18	1.364 (3)	C41B—C41B^{ii}	1.218 (17)
C15—C16	1.378 (3)	C41B—H41B	0.9500
C15—O20	1.368 (2)	C30—O31	1.248 (3)
C16—H16	0.9500	C30—O32	1.246 (3)

C16—C17	1.399 (3)	C30—C33A	1.504 (3)
C17—H17	0.9500	C30—C33B	1.555 (10)
O18—C19	1.432 (2)	C33A—C33A^{iii}	1.322 (8)
C19—H19A	0.9800	C33A—H33A	0.9500
C19—H19B	0.9800	C33B—C33B^{iii}	1.32 (2)
C19—H19C	0.9800	C33B—H33B	0.9500
O20—C21	1.427 (2)		

C2—N1—H1	118.2	O18—C19—H19C	109.5
C2—N1—C10	123.56 (18)	H19A—C19—H19B	109.5
C10—N1—H1	118.2	H19A—C19—H19C	109.5
N1—C2—C3	118.9 (2)	H19B—C19—H19C	109.5
N1—C2—C11	117.53 (17)	C15—O20—C21	116.92 (17)
C3—C2—C11	123.60 (18)	O20—C21—H21A	109.5
C2—C3—C4	121.08 (19)	O20—C21—H21B	109.5
C2—C3—C8	119.45 (18)	O20—C21—H21C	109.5
C8—C3—C4	119.47 (16)	H21A—C21—H21B	109.5
C3—C4—H4	119.8	H21A—C21—H21C	109.5
C5—C4—C3	120.47 (18)	H21B—C21—H21C	109.5
C5—C4—H4	119.8	C5—O22—C23	116.43 (14)
C4—C5—C6	120.03 (17)	O22—C23—H23A	109.5
O22—C5—C4	125.26 (18)	O22—C23—H23B	109.5
O22—C5—C6	114.68 (15)	O22—C23—H23C	109.5
C7—C6—C5	120.41 (16)	H23A—C23—H23B	109.5
O24—C6—C5	113.56 (16)	H23A—C23—H23C	109.5
O24—C6—C7	126.02 (18)	H23B—C23—H23C	109.5
C6—C7—H7	119.9	C6—O24—C25	117.25 (16)
C6—C7—C8	120.11 (19)	O24—C25—H25A	109.5
C8—C7—H7	119.9	O24—C25—H25B	109.5
C3—C8—C9	117.70 (18)	O24—C25—H25C	109.5
C7—C8—C3	119.43 (17)	H25A—C25—H25B	109.5
C7—C8—C9	122.9 (2)	H25A—C25—H25C	109.5
C8—C9—H9	120.0	H25B—C25—H25C	109.5
C10—C9—C8	120.0 (2)	O35—C34—C37	113.63 (18)
C10—C9—H9	120.0	O36—C34—O35	124.4 (2)
N1—C10—C9	120.4 (2)	O36—C34—C37	121.98 (19)
N1—C10—H10	119.8	C34—O35—H35	109.5
C9—C10—H10	119.8	C34—C37—H37	117.7
C2—C11—H11A	109.0	C37^{i}—C37—C34	124.6 (2)
C2—C11—H11B	109.0	C37^{i}—C37—H37	117.7
C2—C11—C12	113.08 (16)	O39A—C38—C41A	116.0 (3)
H11A—C11—H11B	107.8	O39B—C38—O40B	128.8 (6)
C12—C11—H11A	109.0	O39B—C38—C41B	121.7 (6)
C12—C11—H11B	109.0	O40A—C38—O39A	125.4 (3)
C13—C12—C11	119.44 (18)	O40A—C38—C41A	118.6 (3)
C17—C12—C11	121.0 (2)	O40B—C38—C41B	108.9 (6)
C17—C12—C13	119.51 (19)	C38—O39A—H39A	109.5
C12—C13—H13	119.6	C38—O40B—H40B	102 (4)

C14—C13—C12	120.86 (18)	C38—C41A—H41A	118.9
C14—C13—H13	119.6	C41A^{ii}—C41A—C38	122.3 (7)
C13—C14—C15	119.3 (2)	C41A^{ii}—C41A—H41A	118.9
O18—C14—C13	125.05 (18)	C38—C41B—H41B	118.9
O18—C14—C15	115.65 (18)	C41B^{ii}—C41B—C38	122.2 (15)
C16—C15—C14	119.54 (19)	C41B^{ii}—C41B—H41B	118.9
O20—C15—C14	114.80 (19)	O31—C30—C33A	110.7 (2)
O20—C15—C16	125.64 (17)	O31—C30—C33B	145.1 (5)
C15—C16—H16	119.6	O32—C30—O31	122.17 (17)
C15—C16—C17	120.76 (18)	O32—C30—C33A	127.1 (2)
C17—C16—H16	119.6	O32—C30—C33B	92.6 (5)
C12—C17—C16	120.0 (2)	C30—C33A—H33A	119.1
C12—C17—H17	120.0	C33A^{iii}—C33A—C30	121.9 (4)
C16—C17—H17	120.0	C33A^{iii}—C33A—H33A	119.1
C14—O18—C19	117.23 (17)	C30—C33B—H33B	122.1
O18—C19—H19A	109.5	C33B^{iii}—C33B—C30	115.7 (13)
O18—C19—H19B	109.5	C33B^{iii}—C33B—H33B	122.1

N1—C2—C3—C4	−178.96 (16)	C11—C12—C13—C14	177.90 (16)
N1—C2—C3—C8	2.3 (3)	C11—C12—C17—C16	−178.71 (16)
N1—C2—C11—C12	103.3 (2)	C12—C13—C14—C15	0.6 (3)
C2—N1—C10—C9	−1.0 (3)	C12—C13—C14—O18	−178.84 (17)
C2—C3—C4—C5	−177.63 (17)	C13—C12—C17—C16	−0.9 (3)
C2—C3—C8—C7	175.96 (16)	C13—C14—C15—C16	−0.4 (3)
C2—C3—C8—C9	−2.8 (3)	C13—C14—C15—O20	−179.14 (16)
C2—C11—C12—C13	127.20 (19)	C13—C14—O18—C19	−1.7 (3)
C2—C11—C12—C17	−55.0 (2)	C14—C15—C16—C17	−0.5 (3)
C3—C2—C11—C12	−77.7 (2)	C14—C15—O20—C21	−179.53 (17)
C3—C4—C5—C6	1.4 (3)	C15—C14—O18—C19	178.86 (16)
C3—C4—C5—O22	179.76 (16)	C15—C16—C17—C12	1.1 (3)
C3—C8—C9—C10	1.5 (3)	C16—C15—O20—C21	1.8 (3)
C4—C3—C8—C7	−2.8 (3)	C17—C12—C13—C14	0.1 (3)
C4—C3—C8—C9	178.42 (16)	O18—C14—C15—C16	179.10 (16)
C4—C5—C6—C7	−2.2 (3)	O18—C14—C15—O20	0.3 (2)
C4—C5—C6—O24	177.01 (16)	O20—C15—C16—C17	178.15 (16)
C4—C5—O22—C23	−2.8 (3)	O22—C5—C6—C7	179.25 (16)
C5—C6—C7—C8	0.5 (3)	O22—C5—C6—O24	−1.5 (2)
C5—C6—O24—C25	−172.83 (16)	O24—C6—C7—C8	−178.63 (17)
C6—C5—O22—C23	175.66 (18)	O35—C34—C37—C37^{i}	10.4 (3)
C6—C7—C8—C3	2.0 (3)	O36—C34—C37—C37^{i}	−168.9 (2)
C6—C7—C8—C9	−179.28 (17)	O39A—C38—C41A—C41A^{ii}	176.4 (4)
C7—C6—O24—C25	6.3 (3)	O39B—C38—C41B—C41B^{ii}	−12.6 (10)
C7—C8—C9—C10	−177.25 (18)	O40A—C38—C41A—C41A^{ii}	−5.6 (6)
C8—C3—C4—C5	1.1 (3)	O40B—C38—C41B—C41B^{ii}	175.7 (8)
C8—C9—C10—N1	0.4 (3)	O31—C30—C33A—C33A^{iii}	−171.1 (3)
C10—N1—C2—C3	−0.3 (3)	O31—C30—C33B—C33B^{iii}	7.3 (12)
C10—N1—C2—C11	178.75 (18)	O32—C30—C33A—C33A^{iii}	10.5 (4)

C11—C2—C3—C4	2.0 (3)	O32—C30—C33B—C33B^{iii}	−176.6 (8)
C11—C2—C3—C8	−176.73 (16)		

Symmetry codes: (i) −*x*+1, −*y*+2, −*z*; (ii) −*x*+2, −*y*+2, −*z*+2; (iii) −*x*+2, −*y*+2, −*z*+1.

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···O31	0.88	2.20	3.034 (3)	159
N1—H1···O32	0.88	2.18	2.919 (2)	141
O35—H35···O31	0.84	1.83	2.617 (2)	156
O39*A*—H39*A*···O32	0.84	1.67	2.502 (4)	169

Selected geometric parameters (Å) for fumaric acid A, B, and C in compound (I)

C30–O31	1.248 (2)
C30–O32	1.246 (3)
C34–O35	1.324 (3)
C34–O36	1.211 (2)
C38–O39A[a]	1.280 (5)
C38–O40A[a]	1.231 (6)