Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

The *E* and *Z* isomers of 3-(benzoxazol-2-yl)prop-2-enoic acid

Jose G. Trujillo-Ferrara,[a] Itzia I. Padilla-Martínez,[b] Francisco J. Martínez-Martínez,[b] Herbert Höpfl,[c] Norberto Farfan-García[d] and Efrén V. García-Báez[b]*

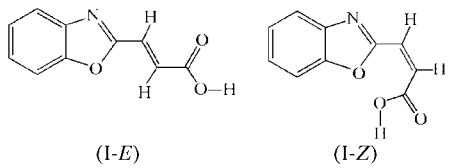
[a]Sección de Graduados y Departamento de Bioquímica, Escuela Superior de Medicina, Instituto Politécnico Nacional, México, DF 11340, Mexico, [b]Unidad Profesional Interdisciplinaria de Biotecnología, Instituto Politécnico Nacional, Avenida Acueducto s/n, Barrio La Laguna Ticomán, México, DF 07340, Mexico, [c]Centro de Investigaciónes Químicas, Universidad Autónoma del Estado de Morelos, Cuernava Morelos, Mexico, and [d]Centro de Investigación y Estudios Avanzados del Instituto Politecnico Nacional, Avenida IPN 2508, México, DF 07330, Mexico
Correspondence e-mail: vgarcia@acei.upibi.ipn.mx

Received 4 June 2004
Accepted 19 July 2004
Online 4 September 2004

The carboxylic acid group and the double bond are coplanar in (*E*)-3-(benzoxazol-2-yl)prop-2-enoic acid, $C_{10}H_7NO_3$, whereas in isomeric (*Z*)-3-(benzoxazol-2-yl)prop-2-enoic acid, also $C_{10}H_7NO_3$, they are almost orthogonal. In both isomers, a strong O—H···N hydrogen bond, with the carboxylic acid group as a donor and the pyridine-like N atom as an acceptor, and weak C—H···O interactions contribute to the observed supramolecular structures, which are completed by π–π stacking interactions between oxazole and benzenoid rings.

Comment

γ-Aminobutyric acid (GABA) is the major inhibitory neurotransmitter in the central nervous system (CNS). GABA operates through three different classes of receptors, consisting of the ionotropic $GABA_A$ and $GABA_C$ receptors, and the G-protein coupled receptor $GABA_B$ (Chebib & Johnston, 2000). Hypoactivity of the GABA neuronal function has been associated with pain and neurological disorders such as epilepsy, Huntington's chorea, anxiety and sleep disorders. In contrast, GABA-mediated hyperactivity has been suggested to be an important component of schizophrenic symptoms (Frølund *et al.*, 2002). In order to characterize these receptors pharmacologically, recent studies of the synthesis



(I-*E*) (I-*Z*)

and characterization of several GABA agonists (Chambers *et al.*, 2003; Frølund *et al.* 1995) and antagonists (Frølund *et al.*, 2002) have been undertaken. GABA is a conformationally flexible molecule, capable of adopting receptor subtype-specific conformations; in this context, we report the results of structural analyses of the *E* and *Z* geometric isomers of 3-(benzoxazol-2-yl)prop-2-enoic acid [(I-*E*) and (I-*Z*), respectively], which are analogues of GABA.

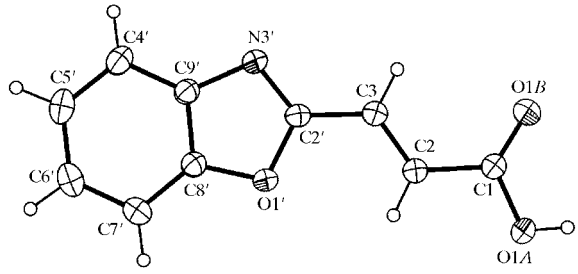


Figure 1
The molecular structure of (I-*E*), showing displacement ellipsoids at the 30% probability level.

A one-pot synthesis was carried out by mixing equimolar quantities of maleic anhydride and *o*-aminophenol in tetrahydrofuran (THF). Careful regulation of the temperature to 323 K, using Ac_2O as catalyst, yielded isomer (I-*Z*); isomer (I-*E*) was obtained when the temperature was raised to 343 K and an excess of Ac_2O was used. It appears that (I-*Z*) is the kinetic product and (I-*E*) is the thermodynamic product, since the former is observed by thin-layer chromatography in the early stages of the reaction. The molecular structures of (I-*E*) and (I-*Z*) are shown in Figs. 1 and 2, respectively, while selected geometric parameters are given in Tables 1 and 3, respectively. The bond lengths and angles are very similar in the two isomers, as is the *anti* disposition of the double bond and the imine group. However, the carboxy and benzoxazole groups are on opposite sides in (I-*E*) and on the same side in (I-*Z*).

The carboxy group in (I-*E*) is coplanar with the double bond, whereas in (I-*Z*) these groups are almost orthogonal [O1*B*—C1—C2—C3 = −4.1 (3) and 103.7 (3)°, respectively], in agreement with the conformation reported for other (*Z*)-propenoic acids (Stomberg *et al.*, 1995). This conformational difference between the isomers determines the observed crystal packing (see below). Isomer (I-*E*) forms

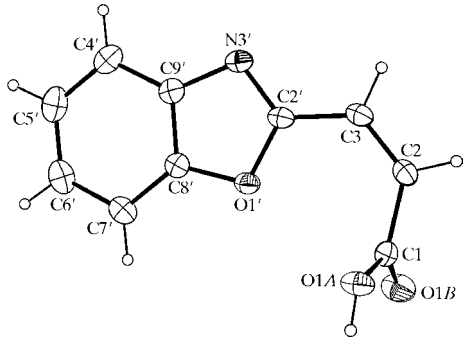


Figure 2
The molecular structure of (I-*Z*), showing displacement ellipsoids at the 30% probability level.

 DOI: 10.1107/S0108270104017743

supramolecular sheets in the $(10\bar{2})$ plane through both strong (Steiner, 2002) and weak (Desiraju, 1996) hydrogen-bonding interactions. The hydrogen-bonding geometry for isomer (I-*E*) is listed in Table 2. The carboxylic acid donor and pyridine-like N-atom acceptor form a strong O1*A*—H1*A*···N3′^{i} interaction [symmetry code: (i) $x-1, \frac{1}{2}-y, -\frac{1}{2}+z$], which is complemented by a weak C5′—H5′···O1*B*^{ii} interaction [symmetry code: (ii) $1-x, y-\frac{1}{2}, \frac{1}{2}-z$] between an aromatic H-atom donor and a carbonyl O-atom acceptor (Fig. 3).

Centrosymmetric sheets pack *via* π–π stacking interactions (Hunter *et al.*, 1991; Singh & Thornton, 1990) between oxazole and benzenoid rings along the *c* axis. The mean intercentroid and interplanar distances [3.707 (1) and 3.435 (1) Å, respectively] at the $(1-x, -y, -z)$ symmetry position indicate a face-to-face π–π stacking arrangement, whereas the distances [4.4487 (11) and 3.38 (2) Å] at the $(1-x, -y, 1-z)$ symmetry position indicate a parallel displaced π–π stacking arrangement. The former arrangement is overwhelmingly preferred in the stacking of electron-rich and electron-deficient aromatic rings, such as benzene and hexafluorobenzene, whose 1:1 complex has mean intercentroid and interplanar distances of 3.7 and 3.4 Å, respectively (Williams, 1993). The electron-deficient carbonyl C atom is located 3.36 (4) Å from the electron-rich double bond of the neighbouring molecule [symmetry code: (v) $x, \frac{1}{2}-y, \frac{1}{2}+z$], forming an angle of 68 (1)° with this double bond (Fig. 3). This distance is as short as the sum of the van der Waals radii of two C atoms (3.4 Å; Hunter *et al.*, 1991), and the carbonyl group is parallel but slightly displaced relative to the double bond. Therefore, this interaction can be considered as a parallel-to-displaced olefin-type π–π stacking interaction (Kim *et al.*, 2000), which should be an important contributor to the slippage of the hydrogen-bonded supramolecular sheets of (I-*E*).

Molecules of (I-*Z*) are linked by a strong hydrogen-bonding interaction [O1*A*—H1*A*···N3′^{vi}; symmetry code: (vi) $\frac{1}{2}+x, \frac{1}{2}+y, z$] between the carboxylic acid donor and the pyridine-like N-atom acceptor, and a weak interaction [C3—H3···O1*B*^{vii}; symmetry code: (vii) $\frac{1}{2}-x, y-\frac{1}{2}, \frac{1}{2}-z$] involving a vinyl H-atom donor and the carbonyl O-atom acceptor (Fig. 4). As a consequence, a twisted eight-membered chain is formed, whose topological motif is described by the $C(8)[C(7)C(5)]$ graph-set descriptor (Bernstein *et al.*, 1995). This interaction is allowed because of the almost perpendicular conformation between the carboxy and double-bond groups. The hydrogen-bonding geometry for (I-*Z*) is listed in Table 4.

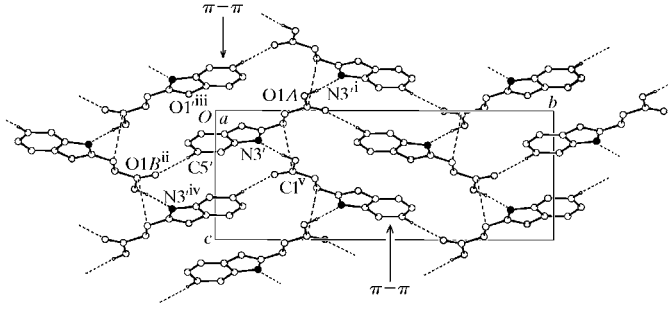


Figure 3
The supramolecular structure of (I-*E*), viewed along the *a* axis. Centrosymmetric sheets of molecules pack through face-to-face and parallel-displaced π–π stacking interactions. [Symmetry codes: (i) $x-1, \frac{1}{2}-y, -\frac{1}{2}+z$; (ii) $1-x, y-\frac{1}{2}, \frac{1}{2}-z$; (iii) $1-x, -y, -z$; (iv) $1-x, -y, 1-z$; (v) $x, \frac{1}{2}-y, \frac{1}{2}+z$.]

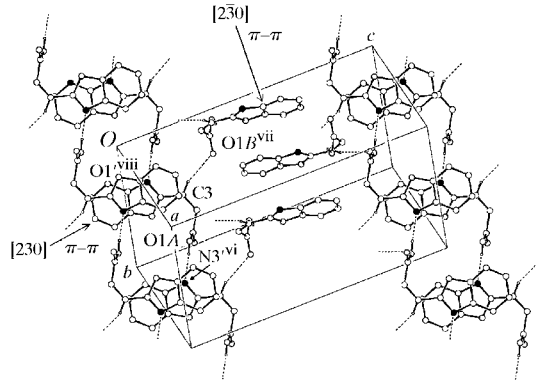


Figure 4
The supramolecular structure of (I-*Z*), viewed along the [230] and [2$\bar{3}$0] directions. [Symmetry codes: (vi) $\frac{1}{2}+x, \frac{1}{2}+y, z$; (vii) $\frac{1}{2}-x, y-\frac{1}{2}, \frac{1}{2}-z$; (viii) $-x, 1-y, -z$.]

Experimental

The title propenoic acid derivatives (I-*Z*) and (I-*E*) were obtained by the reaction between equimolar quantities (1.0 mmol) of maleic anhydride and 2-aminophenol dissolved in THF. Ac_2O (0.1 mmol) was added as catalyst, and after heating at 323–328 K for 2 h, isomer (I-*Z*) was obtained. Under the same conditions, but heating at 343 K for 3 h with acetic anhydride (1.5 mol), isomer (I-*E*) was obtained. In both cases, THF was removed by evaporation and the resulting solid was treated with aqueous HCl (5%) until precipitation was complete. After washing three times with deionized water and drying, the products were recrystallized from ethanol solutions to give crystals suitable for X-ray analysis in approximately 70% yield. For (I-*E*), m.p. 500–502 K; IR (KBr, cm^{-1}): ν 1710 (COO), 1527 (C═N); ^{1}H NMR: δ 13.2 (*b*, 1H, OH), 7.84 (*d*, 1H, ^3J = 8.6 Hz, H4′), 7.77 (*d*, 1H, ^3J = 8.6 Hz, H7′), 7.52 (*dd*, 1H, ^3J = 8.6 Hz, H6′), 7.45 (*d*, 1H, ^3J = 15.8 Hz, H3), 7.44 (*dd*, 1H, ^3J = 8.6 Hz, H5′), 6.92 (*d*, 1H, ^3J = 15.8 Hz, H2); ^{13}C NMR: δ 166.0 (C1), 159.9 (C2′), 150.1 (C8′), 141.4 (C9′), 129.3 (C2), 128.2 (C3), 126.9 (C6′), 125.2 (C5′), 120.5 (C4′), 111.1 (C7′). For (I-*Z*), m.p. 396–397 K; IR (KBr, cm^{-1}): ν 1707 (COO), 1527 (C═N); ^{1}H NMR: δ 13.2 (*b*, 1H, OH), 7.8 (*dd*, 1H, ^3J = 8.5 Hz, ^4J = 1.2 Hz, H4′), 7.7 (*dd*, 1H, ^3J = 8.0 Hz, ^4J = 1.3 Hz, H7′), 7.4 (*ddd*, 1H, ^3J = 8.6 Hz, ^4J = 1.3 Hz, H6′), 7.5 (*ddd*, 1H, ^3J = 8.6 Hz, ^4J = 1.3 Hz, H5′), 6.88 (*d*, 1H, ^3J = 12.0 Hz, H3), 6.66 (*d*, 1H, ^3J = 12.0 Hz, H2); ^{13}C NMR: δ 167.0 (C1), 159.6 (C2′), 149.8 (C8′), 140.1 (C9′), 132.3 (C2), 120.0 (C3), 126.3 (C6′), 125.1 (C5′), 120.1 (C4′), 111.0 (C7′).

Isomer (I-*E*)

Crystal data

$C_{10}H_7NO_3$
$M_r = 189.17$
Monoclinic, $P2_1/c$
$a = 5.882\ (1)$ Å
$b = 19.694\ (1)$ Å
$c = 7.4910\ (1)$ Å
$\beta = 91.715\ (10)^\circ$
$V = 867.37\ (15)$ Å^3
$Z = 4$
$D_x = 1.449$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 24 reflections
$\theta = 10$–11°
$\mu = 0.11$ mm^{-1}
$T = 293\ (2)$ K
Block, yellow
0.50 × 0.50 × 0.40 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
2082 measured reflections
2082 independent reflections
1554 reflections with $I > 2\sigma(I)$
$R_{int} = 0.011$
$\theta_{max} = 28.0^\circ$
$h = -7 \rightarrow 7$
$k = 0 \rightarrow 25$
$l = 0 \rightarrow 9$
3 standard reflections
every 200 reflections
intensity decay: 2.5%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.037$
$wR(F^2) = 0.124$
$S = 1.15$
2082 reflections
128 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.058P)^2 + 0.105P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.19$ e Å^{-3}
$\Delta\rho_{min} = -0.18$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °) for isomer (I-*E*).

O1′—C2′	1.3588 (17)	O1*B*—C1	1.1978 (19)
O1′—C8′	1.3800 (16)	N3′—C2′	1.2987 (17)
O1*A*—C1	1.324 (2)	N3′—C9′	1.3962 (18)
C2′—O1′—C8′	104.23 (10)	N3′—C2′—C3	127.00 (12)
C2′—N3′—C9′	104.76 (11)	O1′—C2′—N3′	114.92 (12)
O1*A*—C1—C2	111.12 (12)	O1′—C8′—C9′	107.77 (12)
O1*B*—C1—C2	124.61 (16)	N3′—C9′—C8′	108.32 (11)
O1*A*—C1—O1*B*	124.25 (14)	N3′—C9′—C4′	131.53 (12)
O1′—C2′—C3	118.08 (11)		
O1′—C2′—C3—C2	2.5 (2)	N3′—C2′—C3—C2	−178.33 (14)

Table 2
Hydrogen-bonding geometry (Å, °) for isomer (I-*E*).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1*A*—H1*A*···N3′^{i}	0.82	1.89	2.6995 (16)	167
C5′—H5′···O1*B*^{ii}	0.93	2.46	3.372 (2)	165

Symmetry codes: (i) $x-1, \frac{1}{2}-y, -\frac{1}{2}+z$; (ii) $1-x, y-\frac{1}{2}, \frac{1}{2}-z$.

Isomer (I-*Z*)

Crystal data

$C_{10}H_7NO_3$
$M_r = 189.17$
Monoclinic, $C2/c$
$a = 9.8191\ (19)$ Å
$b = 9.905\ (2)$ Å
$c = 18.320\ (4)$ Å
$\beta = 94.037\ (4)^\circ$
$V = 1777.4\ (6)$ Å^3
$Z = 8$
$D_x = 1.414$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 1010 reflections
$\theta = 1.6$–32.0°
$\mu = 0.11$ mm^{-1}
$T = 293\ (2)$ K
Block, yellow
0.36 × 0.21 × 0.19 mm

Data collection

Bruker *SMART* area-detector diffractometer
φ and ω scans
9736 measured reflections
2013 independent reflections
1559 reflections with $I > 2\sigma(I)$
$R_{int} = 0.035$
$\theta_{max} = 27.5^\circ$
$h = -12 \rightarrow 12$
$k = -12 \rightarrow 12$
$l = -23 \rightarrow 23$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.053$
$wR(F^2) = 0.127$
$S = 1.05$
2013 reflections
128 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.045P)^2 + 1.031P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.23$ e Å^{-3}
$\Delta\rho_{min} = -0.18$ e Å^{-3}

Table 3
Selected geometric parameters (Å, °) for isomer (I-*Z*).

O1′—C2′	1.359 (2)	O1*B*—C1	1.200 (2)
O1′—C8′	1.382 (2)	N3′—C2′	1.298 (2)
O1*A*—C1	1.305 (2)	N3′—C9′	1.399 (3)
C2′—O1′—C8′	104.51 (13)	O1′—C2′—C3	119.65 (15)
C2′—N3′—C9′	105.13 (15)	N3′—C2′—C3	125.74 (17)
O1*A*—C1—C2	113.76 (16)	O1′—C2′—N3′	114.59 (16)
O1*B*—C1—C2	121.59 (18)	O1′—C8′—C7′	128.29 (17)
O1*A*—C1—O1*B*	124.57 (18)	N3′—C9′—C4′	131.94 (18)
O1*A*—C1—C2—C3	−79.5 (3)	O1′—C2′—C3—C2	−3.2 (3)
O1*B*—C1—C2—C3	103.7 (3)	N3′—C2′—C3—C2	178.51 (19)

Table 4
Hydrogen-bonding geometry (Å, °) for isomer (I-*Z*).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1*A*—H1*A*···N3′^{vi}	0.82	1.90	2.715 (2)	172
C3—H3···O1*B*^{vii}	0.93	2.43	3.310 (3)	159

Symmetry codes: (vi) $\frac{1}{2}+x, \frac{1}{2}+y, z$; (vii) $\frac{1}{2}-x, y-\frac{1}{2}, \frac{1}{2}-z$.

All H atoms were refined as riding on their parent atoms using *SHELXL*97 (Sheldrick, 1997) defaults [O—H = 0.82 Å, C—H = 0.93 Å and $U_{iso}(H) = 1.2U_{eq}(C,O)$].

For (I-*E*), data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1992); cell refinement: *CAD*-4 *EXPRESS*; data reduction: *JANA*98 (Vaclav, 1998); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *WinGX* (Farrugia, 1999); software used to prepare material for publication: *SHELXL*97.

For (I-*Z*), data collection: *SMART* (Bruker, 2000); cell refinement: *SAINT* (Bruker, 2000); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS*97; program(s) used to refine structure: *SHELXL*97; molecular graphics: *SHELXTL* (Bruker, 2000); software used to prepare material for publication: *SHELXL*97 and *WinGX*.

This work was supported by the CGPI–IPN (Coordinación General de Posgrado e Investigación del Instituto Politécnico Nacional).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM1572). Services for accessing these data are described at the back of the journal.

References

Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.

Bruker (2000). *SMART*, *SAINT* and *SHELXTL*. Bruker AXS Inc., Madison, Wisconsin, USA.

Chambers, M. S., Atack, J. R., Broughyon, H. B., Collinson, N., Dawson, G. R., Hobbs, S. C., Marshall, G., Maubach, K. A., Pillai, G. V., Reeve, A. J. & Macleed, A. (2003). *J. Med. Chem.* **46**, 2227–2240.

Chebib, M. & Johnston, G. A. R. (2000). *J. Med. Chem.* **43**, 1427–1447.

Desiraju, G. R. (1996). *Acc. Chem. Res.* pp. 441–449.

Enraf–Nonius (1992). *CAD*-4 *EXPRESS*. Version 5.1. Enraf–Nonius, Delft, The Netherlands.

Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.

Frølund, B., Jørgensen, A. T., Tagmose, L., Stensbøl, T. B., Vestergaard, H. T., Engblom, C., Kristiansen, U., Sanchez, C., Krogsgaard-Larsen, P. & Liljefors, T. (2002). *J. Med. Chem.* **45**, 2454–2468.

Frølund, B., Kristiansen, U., Brehm, L., Hansem, A. B., Krogsgaard-Larsen, P. & Falch, E. (1995). *J. Med. Chem.* **38**, 3287–3296.

Hunter, C. A., Singh, J. & Thornton, J. M. (1991). *J. Mol. Biol.* **218**, 837–846.

Kim, K. S., Tarakeshwar, P. & Lee, J. Y. (2000). *Chem. Rev.* **100**, 4145–4185.

Sheldrick, G. M. (1997). *SHELXS*97 and *SHELXL*97. University of Göttingen, Germany.

Singh, J. & Thornton, J. M. (1990). *J. Mol. Biol.* **211**, 595–515.

Steiner, T. (2002). *Angew. Chem. Int. Ed.* **41**, 48–76.

Stomberg, R., Li, S. & Lundquist, K. (1995). *Acta Cryst.* C**51**, 2698–2700.

Vaclav, P. (1998). *JANA*98. Institute of Physics AVCR, Cukravarnicka, 10 162 53 Prague, Czech Republic.

Williams, J. H. (1993). *Acc. Chem. Res.* **26**, 593–598.