

Kai Chen, S. James Adelstein and  
Amin I. Kassis\*Department of Radiology, Harvard Medical  
School, 200 Longwood Ave, Armenise Building,  
D2-137, Boston, MA 02115, USACorrespondence e-mail:  
amin\_kassis@hms.harvard.edu

## Key indicators

Single-crystal X-ray study  
 $T = 193\text{ K}$   
Mean  $\sigma(\text{C}-\text{C}) = 0.004\text{ \AA}$   
 $R$  factor = 0.031  
 $wR$  factor = 0.066  
Data-to-parameter ratio = 18.7For details of how these key indicators were  
automatically derived from the article, see  
<http://journals.iucr.org/e>.

## (2E)-2-(3,5-Dimethoxyphenyl)-3-(4-ethoxy-3-iodo-phenyl)acrylic acid

The X-ray analysis of the title compound,  $\text{C}_{19}\text{H}_{19}\text{IO}_5$ , shows that the orientation of the two benzene rings is *cis* and confirms the *E* configuration of the molecule. The occurrence of  $\text{O}-\text{H}\cdots\text{O}$  hydrogen-bonding interactions results in the formation of centrosymmetric dimers.

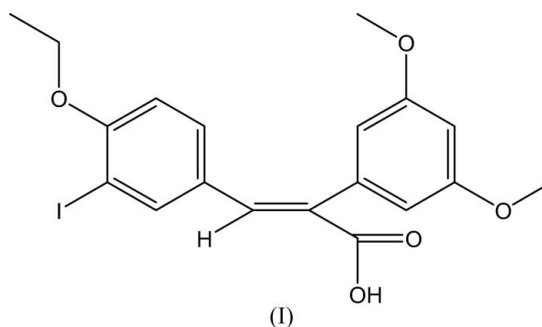
Received 15 September 2005

Accepted 26 September 2005

Online 30 September 2005

## Comment

Since the position of an Auger electron emitter (e.g.  $^{77}\text{Br}$ ,  $^{123}\text{I}$  or  $^{125}\text{I}$ ) *vis à vis* DNA is of paramount importance for DNA double-strand-break yield and toxicity (Kassis, 2004), the development of a carrier molecule locating the Auger electron emitter in close proximity to the nuclear DNA of cells is of great interest. We have recently focused on the synthesis of Hoechst-skeleton-based ligands, designed by *in silico* methods (Chen *et al.*, 2004*a,b*), with predictable iodine-to-DNA distances. The title compound, (I), has been produced as an important intermediate, and its configuration has been determined by X-ray structure analysis and is presented here.



As shown in Fig. 1, the orientation of the two benzene rings is *cis*, thus clearly demonstrating that the configuration of compound (I) is *E*. The  $\text{C}1-\text{C}2-\text{C}3-\text{C}10$  and  $\text{C}2-\text{C}3-\text{C}10-\text{C}11$  torsion angles are  $174.7(3)$  and  $169.0(3)^\circ$ , respectively, indicating that the iodine-substituted benzene ring and the acrylic acid group are nearly coplanar, whereas the dimethoxy-substituted benzene ring is inclined to this plane, with a dihedral angle of  $72.50(7)^\circ$  between planes  $\text{C}4-\text{C}9$  and  $\text{C}10-\text{C}15$ . In the crystal structure, strong intermolecular  $\text{O}-\text{H}\cdots\text{O}$  hydrogen bonds (Table 1) connect the molecules, producing distinct dimers arranged around inversion centres (Fig. 2).

## Experimental

To a solution of 4-ethoxy-3-iodobenzaldehyde (2 mmol), prepared according to the method of Harapanhalli *et al.* (1996), and (3,5-dimethoxyphenyl)acetic acid (2 mmol) in acetic anhydride (10 ml), triethylamine (4 mmol) was added dropwise and the solution was

stirred at 363 K for 6 h. Water (6 ml) was then added and the reaction was allowed to continue for 30 min, after which  $K_2CO_3$  (8 mmol) in water (10 ml) was added dropwise and the reaction warmed to 333 K. The reaction was stirred for an additional 30 min, then cooled to 283 K, and acidified to pH 3 with 6 M HCl. The aqueous solution was extracted with  $CH_2Cl_2$  ( $3 \times 15$  ml), and the organic phases were combined, washed with brine ( $3 \times 15$  ml), and dried. The solution was then concentrated under reduced pressure and the residue was recrystallized from ethanol to afford compound (I) (yield: 80%, m.p. 480 K).  $^1H$  NMR ( $d_6$ -DMSO, 200 MHz):  $\delta$  7.61 (s, 1H), 7.53 (s, 1H), 7.12 (d, 1H), 6.85 (d, 1H), 6.52 (s, 1H), 6.31 (s, 2H), 4.06 (q,  $J = 6.6$  Hz, 2H), 3.71 (s, 6H), 1.31 (t,  $J = 6.6$  Hz, 3H). HR-MS (ESI), calculated for  $C_{19}H_{19}IO_5$ :  $[M+Na]^+$  477.0169; found: 477.0188. Crystals suitable for single-crystal X-ray diffraction were obtained by evaporation of an ethanol solution at 298 K.

Crystal data

$C_{19}H_{19}IO_5$   $D_x = 1.624$  Mg m $^{-3}$   
 $M_r = 454.26$  Mo  $K\alpha$  radiation  
 Monoclinic,  $P2_1/n$  Cell parameters from 978 reflections  
 $a = 12.688$  (2) Å  $\theta = 3.1$ – $27.9^\circ$   
 $b = 11.1649$  (19) Å  $\mu = 1.75$  mm $^{-1}$   
 $c = 14.229$  (2) Å  $T = 193$  (2) K  
 $\beta = 112.861$  (2) $^\circ$  Chunk, yellow  
 $V = 1857.4$  (5) Å $^3$   $0.20 \times 0.16 \times 0.12$  mm  
 $Z = 4$

Data collection

Bruker SMART CCD area detector 4310 independent reflections  
 diffractometer 4085 reflections with  $I > 2\sigma(I)$   
 $\omega$  scans  $R_{int} = 0.015$   
 Absorption correction: multi-scan  $\theta_{max} = 27.9^\circ$   
 (SADABS; Sheldrick, 1996)  $h = -16 \rightarrow 16$   
 $T_{min} = 0.665$ ,  $T_{max} = 0.811$   $k = -9 \rightarrow 14$   
 11524 measured reflections  $l = -18 \rightarrow 17$

Refinement

Refinement on  $F^2$   $w = 1/[\sigma^2(F_o^2) + (0.0209P)^2 + 1.9018P]$   
 $R[F^2 > 2\sigma(F^2)] = 0.031$  where  $P = (F_o^2 + 2F_c^2)/3$   
 $wR(F^2) = 0.066$   $(\Delta\sigma)_{max} = 0.001$   
 $S = 1.20$   $\Delta\rho_{max} = 0.94$  e Å $^{-3}$   
 4310 reflections  $\Delta\rho_{min} = -0.85$  e Å $^{-3}$   
 230 parameters  
 H-atom parameters constrained

Table 1

Hydrogen-bond geometry (Å,  $^\circ$ ).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$O2-H2\cdots O3^i$	0.84	1.79	2.617 (3)	169

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

All H atoms were initially located in a difference Fourier map but they were treated as riding on their parent atoms, with C–H distances of 0.99 (CH $_2$ ), 0.98 (CH $_3$ ) and 0.95 Å (aromatic), and an O–H distance of 0.84 Å, with  $U_{iso}(H) = 1.5U_{eq}(\text{methyl C})$  and  $1.2U_{eq}(C,O)$ .

Data collection: *ASTRO* (Bruker, 1997) and *SMART* (Bruker, 2001); cell refinement: *SMART*; data reduction: *SAINT* (Bruker, 2001); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPIII* (Burnett & Johnson, 1996) and *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97*.

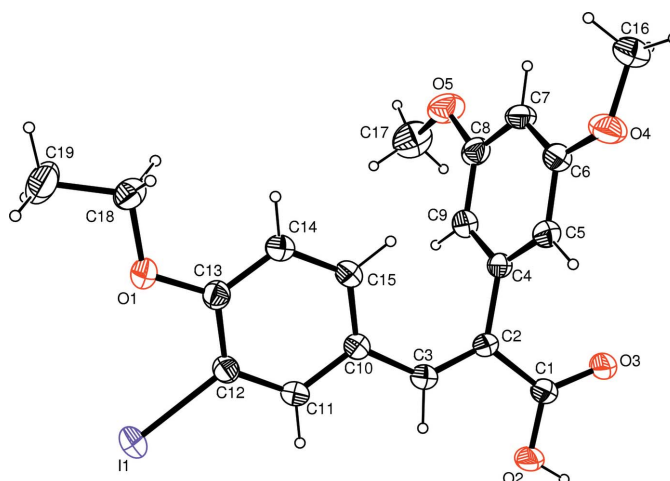


Figure 1

View of the molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are represented by circles of arbitrary size.

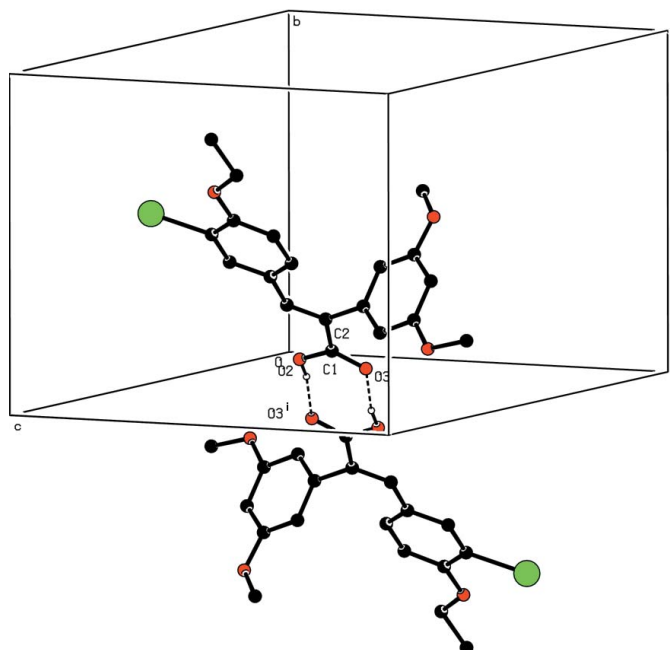


Figure 2

A molecular view of the dimer resulting from the O–H...O hydrogen bonds. H atoms bonded to C atoms have been omitted for clarity. Dashed lines indicate the hydrogen-bonding interactions [symmetry code: (i)  $1 - x, -y, 1 - z$ ].

The authors acknowledge support from NIH grant 5R01CA15523 to AIK, and Dr Richard J. Staples, Department of Chemistry and Chemical Biology, Harvard University, Cambridge, Massachusetts, for helpful discussions.

References

Bruker (1997). *ASTRO* (Version 5.007). Bruker AXS Inc., Madison, Wisconsin, USA.  
 Bruker (2001). *SMART* (Version 5.625) and *SAINT* (Version 6.22). Bruker AXS Inc., Madison, Wisconsin, USA.

- Burnett, M. N. & Johnson, C. K. (1996). *ORTEP*III. Report ORNL-6895. Oak Ridge National Laboratory, Tennessee, USA.
- Chen, K., Adelstein, S. J. & Kassis, A. I. (2004a). *Int. J. Radiat Biol.* **80**, 921–926.
- Chen, K., Adelstein, S. J. & Kassis, A. I. (2004b). *J. Mol. Struct. (Theochem)*, **711**, 49–56.
- Harapanhalli, R. S., McLaughlin, L. W., Howell, R. W., Rao, D. V., Adelstein, S. J. & Kassis, A. I. (1996). *J. Med. Chem.* **39**, 4804–4809.
- Kassis, A. I. (2004). *Int. J. Radiat Biol.* **80**, 789–803.
- Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.
- Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
- Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.