Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

Fenofibrate

R. F. Henry,[a]* G. Z. Zhang,[b] Y. Gao[c] and I. S. Buckner[d]

[a]Abbott Laboratories, Global Pharmaceuticals Division, Department 418, Building AP9, 100 Abbott Park Road, Abbott Park, IL 60064, USA, [b]Abbott Laboratories, Global Pharmaceuticals Division, Department R4P3, Building AP9, 100 Abbott Park Road, Abbott Park, IL 60064, USA, [c]Abbott Laboratories, Global Pharmaceuticals Division, Department D4P#, Building AP9, 100 Abbott Park Road, Abbott Park, IL 60064, USA, and [d]Abbott Laboratories, Global Pharmaceuticals Division, Department D4P3, Building AP9, 100 Abbott Park Road, Abbott Park, IL 60064, USA

Correspondence e-mail: rodger.henry@abbott.com

Key indicators

Single-crystal X-ray study
T = 193 K
Mean σ(C–C) = 0.002 Å
R factor = 0.052
wR factor = 0.147
Data-to-parameter ratio = 18.4

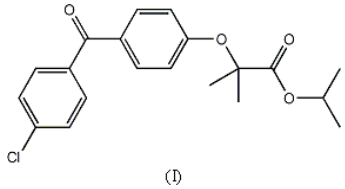
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 24 March 2003
Accepted 14 April 2003
Online 30 April 2003

The crystal structure of 1-methylethyl 2-[4-(4-chlorobenzoyl)-phenoxy]-2-methylpropanoate, also known as fenofibrate, $C_{20}H_{21}ClO_4$, has been determined and is presented here. The compound crystallizes in space group $P\overline{1}$ and is notable for its lack of hydrogen-bond donors and thus a lack of hydrogen bonding.

Comment

Fenofibrate belongs to a class of compounds, fibric acid derivatives, which are used to treat hypercholesterolemia or mixed dyslipidemia (Kloer, 1987). The physicochemical properties of fenofibrate, including solubility, hygroscopicity, distribution coefficient, and solid-state characterization, have been studied in detail (Shoji *et al.*, 1995). Recently, a metastable polymorph was reported (Di Martino *et al.* 2000); in that paper the original polymorph and the newly discovered polymorph were designated forms I and II, respectively. In this paper, we report the molecular structure of fenofibrate form I.



(I)

Fenofibrate form I (see Scheme) crystallizes in the centrosymmetric triclinic space group $P\overline{1}$. The molecule lacks hydrogen-bond donating groups, making it impossible for the structure to contain any type of hydrogen bonding. In the absence of hydrogen-bonding interactions, the molecules are arranged head-to-head and tail-to-tail, producing aliphatic and aromatic layers. These layers are perpendicular to the c axis. An interesting feature of the conformation of the molecule is the symmetrical nature of the isopropyl ester. A survey of the CSD (Allen, 2002) found 115 structures containing isopropyl esters. These 115 structures contained a total of 171 isopropyl ester fragments. The symmetry of the isopropyl ester was measured as the torsion angle between the carbonyl carbon, esteric sp^3 oxygen, isopropyl methine carbon and the centroid of the two methyl groups. Values near zero or 180° would indicate a highly symmetric orientation of the isopropyl group. In this orientation, the isopropyl group's bisecting mirror plane coincides with the plane of the two O atoms and one carbon of the carbonyl group. The mean value found for this torsion angle was 150.7°. The value nearest 180° was 174.6° (Newkome *et al.*, 1985). The corresponding torsion angle in fenofibrate is 178.0°, making it the most symmetric crystallographically characterized isopropyl ester.

Experimental

Crystals were grown by slow evaporation of an ethanol solution.

Crystal data

$C_{20}H_{21}ClO_4$	$Z = 2$
$M_r = 360.82$	$D_x = 1.285$ Mg m^{-3}
Triclinic, $P\overline{1}$	Mo $K\alpha$ radiation
$a = 8.1605$ (16) Å	Cell parameters from 6105 reflections
$b = 8.2664$ (16) Å	$\theta = 2.5$–$28.3°$
$c = 14.511$ (3) Å	$\mu = 0.23$ mm^{-1}
$\alpha = 93.951$ (3)°	$T = 193$ K
$\beta = 105.664$ (3)°	Parallelepiped, colourless
$\gamma = 96.002$ (3)°	0.4 × 0.4 × 0.4 mm
$V = 932.5$ (3) Å^3	

Data collection

Bruker SMART Apex CCD diffractometer	3694 reflections with $I > 2\sigma(I)$
	$R_{int} = 0.065$
ω scans	$\theta_{max} = 28.3°$
Absorption correction: none	$h = -9 \rightarrow 10$
6105 measured reflections	$k = -10 \rightarrow 10$
4225 independent reflections	$l = -19 \rightarrow 19$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.1706P)^2 + 0.7796P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.052$	$(\Delta/\sigma)_{max} = 0.001$
$wR(F^2) = 0.147$	$\Delta\rho_{max} = 0.38$ e Å^{-3}
$S = 1.06$	$\Delta\rho_{min} = -0.34$ e Å^{-3}
4225 reflections	
230 parameters	
H-atom parameters constrained	

H atoms were treated as riding atoms (C—H = 0.93 and 0.97 Å). U_{iso} values for H atoms were fixed at 1.2 times U_{eq} of the parent atom.

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT-Plus* (Bruker, 1999); data reduction: *SAINT-Plus* (Bruker, 1999); program(s) used to solve structure: *SHELXTL* (Sheldrick, 2000); program(s) used to refine structure: *SHELXTL*; molecular graphics: *ORTEP*II (Johnson, 1976).

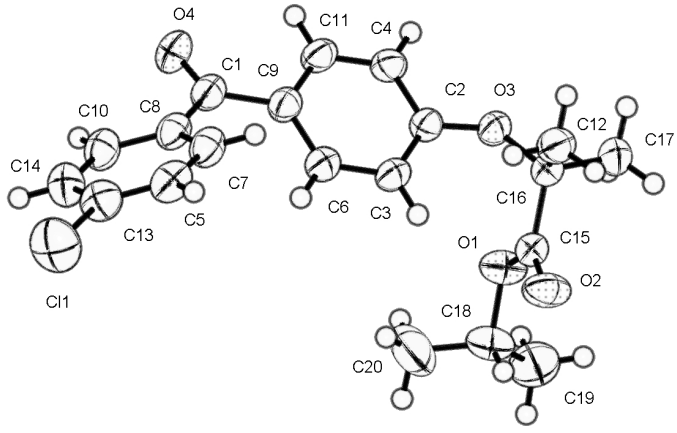


Figure 1
A view of fenofibrate, with the atomic numbering scheme. Displacement ellipsoids are drawn at the 30% probability level.

References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Bruker (1999). *SAINT-Plus.* Version 6.02. Bruker AXS Inc., Madison, Wisconsin, USA.
Bruker (2001). *SMART*. Version 5.624. Bruker AXS Inc., Madison, Wisconsin, USA.
Di Martino, P., Palmieri, G. F. & Martelli S. (2000). *Pharmazie*, **55**, 625–626.
Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee. USA.
Kloer, H. U. (1987). *Am. J. Med.* **83** (suppl 5B), 3–8.
Newkome, G. R., Puckett, W. E., Kiefer, G. E., Gupta, V. K., Fronczek, F. R., Pantaleo, D. C., McClure, G. L., Simpson, J. B. & Deutsch, W. A. (1985). *Inorg. Chem.* **24**, 811.
Sheldrick, G. M. (2000). *SHELXTL.* Version 6.10. Bruker AXS Inc., Madison, Wisconsin, USA.
Shoji, R., Watanabe, T., Tashiro, S. & Shi, S. (1995). *Iyakuhin Kenkyu*, **26**, 386–397.