general, have been increasingly recognized as being of importance in stabilizing organic crystal structures (Taylor & Kennard, 1984; Sarma & Desiraju, 1986). In the crystal structure of enone (1), these bonds are of two types: (*a*) to carbonyl oxygen, O(1)(x,y,z)$\cdots$ C(12)($-x,2-y,1-z$) 3·10 Å; O(1)(x,y,z)$\cdots$H(12a)-($-x,2-y,1-z$) 2·34 Å; C(12)–H(12a)$\cdots$O(1) 127·4°; H(12a)$\cdots$O(1)–C(2) 167·8°; (*b*) to ethereal oxygen O(2)(x,y,z)$\cdots$C(15)($1-x,2-y,2-z$) 3·52 Å; O(2)-(x,y,z)$\cdots$H(15b)($1-x,2-y,2-z$) 2·45 Å; C(15)–H(15b)$\cdots$O(2) 168·4°. The directional preferences of both these bonds seem to be pronounced, in keeping with trends earlier observed (Taylor & Kennard, 1984).

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Structure of WF-3681, 3-(2,5-Dihydro-4-hydroxy-5-oxo-3-phenyl-2-furyl)propionic Acid

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Abstract. $C_{13}H_{12}O_5$, $M_r = 248·24$, monoclinic, $C2/c$, $a = 18·757$ (8), $b = 7·282$ (2), $c = 17·511$ (8) Å, $\beta = 91·20$ (3)°, $V = 2391$ (3) Å^3, $Z = 8$, $D_x = 1·379$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, $\mu = 0·859$ mm^{-1}, $F(000) = 1040$, $T = 293$ K. Final $R = 0·054$ for 1409 unique observed reflections. The molecule contains two planar regions which differ in orientation by 5·7°. Distances from the carbonyl carbons to the center of the phenyl ring are not in the range found in the crystal structures of other potent aldose reductase inhibitor molecules.

Introduction. The crystal structure of the title compound, WF-3681 (Uchida, Itoh, Namiki, Nishikawa & Hashimoto, 1986; Okamoto, Uchida, Umehara, Kohsaka & Imanaka, 1984), has been determined as part of a study of structure–activity relationships of inhibitors of the enzyme aldose reductase. This enzyme, which catalyzes the reduction of glucose to sorbitol, has been implicated in the occurrence of numerous complications of diabetes including cataract formation (Kinoshita, 1974; Kinoshita, Kador & Datiles, 1981; Judzewitsch *et al.*, 1983). Effective inhibitors of aldose reductase are therefore of great pharmacological interest.

A structurally diverse group of compounds will inhibit aldose reductase, apparently at a common site (Kador & Sharpless, 1983). The mechanism of action and crucial structural features of these inhibitors are unknown. In a previous paper (Kissinger, Adman, Clark & Stenkamp, 1985), we have described the structure of the potent aldose reductase inhibitor, sorbinil. Here we describe the structure of WF–3681, an effective inhibitor of the enzyme which differs from other known inhibitors in containing a lactone ring.

Experimental. Sample of the compound provided by Fujisawa Pharmaceutical Co. Ltd as a gift. Crystallized by slow evaporation from ethanol and water solution. Crystal dimensions 0·50 × 0·25 × 0·15 mm. KRISEL control-updated Picker FACS-1 diffractometer. Nickel-filtered Cu $K\alpha$ radiation. Cell constants determined by least squares from angular settings of 20 reflections ($9 < 2\theta < 72°$). ω–2θ scans, 2° min^{-1}. Maximum $(\sin\theta)/\lambda = 0·5451$ Å^{-1} ($0 \le h \le 20$, $-7 \le k \le 0$, $0 \le l \le 18$). Data set of 1837 reflections, 1618 unique, 1409 with $F > 3\sigma_F$. 16 standard reflections collected every 8 h showed <2% variation in intensity. No deterioration correction. Empirical absorption correction (North, Phillips & Mathews, 1968) applied (correction factor 1·01–1·09).

Lorentz–polarization corrections applied. Structure solved by direct methods using *RANTAN*80 (Yao,

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1981). Full-matrix least-squares refinement on F. Function minimized $\sum w(|F_o| - |F_c|)^2$; $w = 1/\sigma_F^2$ based on counting statistics. Anisotropic temperature factors for non-hydrogen atoms, isotropic temperature factors for H atoms. H atoms located in a difference map. $R = 0.054$ (for 1409 reflections with $F > 3\sigma_F$), $wR = 0.071$, goodness of fit = 4.97. Max. $\Delta/\sigma = 0.021$. Min. and max. heights in final difference Fourier map were -0.15 and 0.16 e Å^{-3}, respectively. Isotropic extinction parameter (Larson, 1967) refined to a value of 0.0072 (3). Scattering factors for C and O from Cromer & Mann (1968) and for H from Stewart, Davidson & Simpson (1965). Refinement using programs from *XRAY76* (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976).

Discussion. The final atomic parameters are listed in Table 1 and a view of the molecule with labeled atoms is shown in Fig. 1. Bond lengths and angles in the compound do not differ significantly from accepted values.*

The five-membered lactone ring assumes an envelope conformation. The fragment of the ring containing atoms O(3)–C(5)–C(6)–C(7) is approximately planar [maximum deviation of an atom from the least-squares plane through the four ring atoms is 0.005 (3) Å]. Atom C(4) is located 0.103 (4) Å from the plane of the other four ring atoms. All relevant bond lengths are consistent with a conjugated system consisting of atoms O(3), C(5), O(4), C(6), O(5) and C(7). The phenyl ring is approximately planar [maximum deviation of an atom from the least-squares plane is 0.010 (3) Å] with an average C–C bond distance of 1.387 Å. The angle between the least-squares planes of the phenyl ring and the planar fragment of the lactone ring is 5.7 (7)°. The near coplanarity of these two structural groups and the short length of the C(7)–C(8) bond [1.461 (4) Å] suggest that the π conjugation extends between the groups. Such an extended conjugated system is characteristic of many aldose reductase inhibitors, including numerous flavone derivatives, and is consistent with the observation that most inhibitors of aldose reductase contain a large planar or nearly planar region containing one or more aromatic rings (Kador & Sharpless, 1983).

Another characteristic feature of aldose reductase inhibitor molecules is a carbonyl carbon at a distance of 2.8–3.8 Å from the center of an aromatic ring (Kador & Sharpless, 1983). In the crystal structure of WF-3681, this is not seen. Atom C(5) is 5.125 (3) Å from the center of the phenyl ring. The distance of atom C(1) from the center of the phenyl ring is 5.990 (3) Å. [The distances of these atoms from the center of the lactone ring are 1.192 (3) and 4.366 (3) Å, respectively.] Freedom of motion of the torsion angles around atoms C(2) and C(3) allows the possibility of a low-energy conformation in solution or at the active site for which the C(1) to aromatic ring distance is in the above-mentioned range.

Table 1. *Final positional and equivalent isotropic thermal parameters with e.s.d.'s in parentheses* ($\times 10^4$ *for x, y, z and* $\times 10^3$ *for* U_{eq})

$U_{eq} = (U_{11} + U_{22} + U_{33})/3$.

	x	y	z	U_{eq}(Å^2)
C(1)	6237 (1)	−2055 (4)	−3119 (2)	53
C(2)	6022 (2)	−2468 (6)	−2322 (2)	59
C(3)	6638 (2)	−2468 (5)	−1735 (2)	57
C(4)	6905 (2)	−558 (5)	−1528 (2)	53
C(5)	6472 (1)	814 (5)	−457 (2)	55
C(6)	7202 (1)	198 (4)	−284 (2)	49
C(7)	7485 (1)	−528 (4)	−914 (2)	48
C(8)	8205 (1)	−1201 (4)	−1049 (2)	50
C(9)	8415 (2)	−1718 (5)	−1779 (2)	59
C(10)	9100 (2)	−2327 (5)	−1902 (2)	73
C(11)	9587 (2)	−2436 (5)	−1301 (2)	78
C(12)	9397 (2)	−1906 (5)	−583 (2)	72
C(13)	8710 (2)	−1278 (5)	−451 (2)	61
O(1)	5693 (1)	−2127 (4)	−3609 (1)	69
O(2)	6847 (1)	−1688 (3)	−3309 (1)	62
O(3)	6308 (1)	430 (3)	−1194 (1)	61
O(4)	6051 (1)	1580 (4)	−47 (1)	68
O(5)	7504 (1)	454 (3)	417 (1)	56

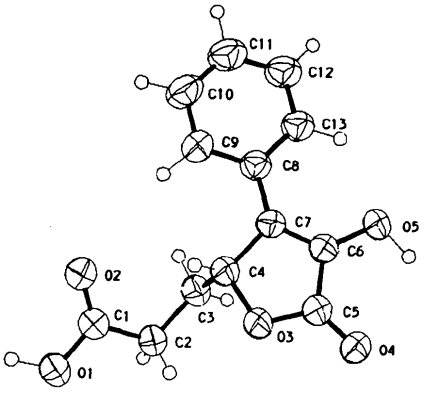

Fig. 1. View of the molecule showing the atomic numbering scheme. The ellipsoids are drawn at the 50% probability level.

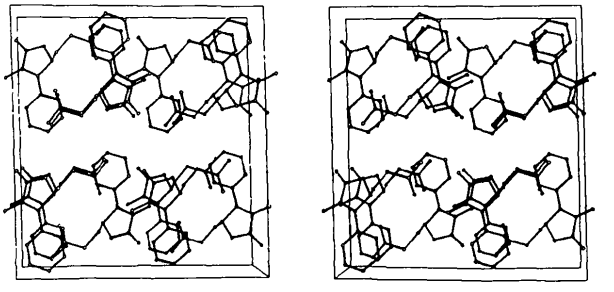

Fig. 2. View of the unit cell down the *b* axis. The *c* axis is horizontal.

* Lists of structure factors, anisotropic thermal parameters, bond lengths and angles and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44317 (21 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

The molecular packing in the crystal is shown in Fig. 2. The molecules stack in the direction of the *b* axis. Pairs of hydrogen bonds occur between molecules of opposite configuration [O(2)···O(5) 2·723 (3), O(2)···H(7) 1·72 (5) Å, O(2)···H(7)–O(5) 174 (4)° and O(4)···O(1) 2·650 (3), O(4)···H(1) 1·65 (4) Å, O(4)···O(1)–H(1) 145 (4)°]. There are no other non-hydrogen contacts between molecules of less than 3·2 Å.

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Structure of Metal-Free Phthalocyanine Stabilized by the Addition of its 4-Chloro Derivative

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Abstract. 1:1 mixture of phthalocyanine ($C_{32}H_{18}N_8$) and 4-chlorophthalocyanine ($C_{32}H_{17}ClN_8$), averaged $M_r = 531$, monoclinic, $C2/n$, $a = 26{\cdot}460\ (1)$, $b = 3{\cdot}760\ (2)$, $c = 24{\cdot}275\ (1)$ Å, $\beta = 93{\cdot}53\ (1)°$, $V = 2410{\cdot}2\ (2)$ Å^3, $Z = 4$, $D_m = 1{\cdot}47$, $D_x = 1{\cdot}465$ Mg m^{-3}, Cu $K\alpha$, $\lambda = 1{\cdot}5418$ Å, $\mu = 7{\cdot}167$ mm^{-1}, averaged $F(000) = 548$, $T = 298$ K, final $R = 0{\cdot}065$ for 1076 independent reflections. The chlorinated molecules occupy the lattice sites at random. The substitution of an H with a Cl occurs at one of the four equivalent molecular sites of 4, 4′, 12 and 12′ with an equal probability for each. The molecule, therefore, looks like a 4,4′,12,12′-tetrachloro derivative in projection. The occupancy of Cl at each site is one-eighth because of the mixing with non-chlorinated molecules in the ratio of 1:1.

Introduction. Phthalocyanine and some of its metal derivatives have at least two crystal forms, the α and β forms (Robertson, 1935, 1936; Brown, 1968*a*). The α form does not grow to a large enough size for X-ray structure analysis. It transforms into the stable β form by heat treatment or in some organic solvents (Moser & Thomas, 1963). The crystal structure of the α form has

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