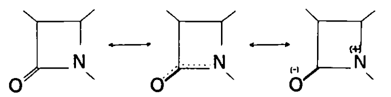
the amount of delocalization of the lone pair as well as steric factors. In the present compound there is no restraint on delocalization of the lone pair on N(1) over C(2) and N(1) atoms, which are conjugated with the C=O bond (Sweet, 1972). This can be expected to make enzymatic attack at the C—N bond less likely.



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Structure of RG-12561 Dichloromethane Solvate and a Diastereomer

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Abstract. (III): [4α,6β(*E*)]-(±)-6-{2-[2-(4-Fluoro-3-methylphenyl)-4,4,6,6-tetramethyl-1-cyclohexen-1-yl]ethenyl}-4-hydroxytetrahydropyran-2-one (RG-12561) dichloromethane solvate, $2C_{24}H_{31}FO_3.CH_2Cl_2$, $M_r = 857.94$, triclinic, $P\bar{1}$, $a = 11.7413\,(5)$, $b = 13.0279\,(5)$, $c = 16.2332\,(9)$ Å, $\alpha = 99.456\,(4)$, $\beta = 94.217\,(4)$, $\gamma = 101.893\,(4)°$, $V = 2381.9\,(4)$ Å^3, $Z = 4$ [four molecules of (III) + two molecules of solvent per unit cell], $D_x = 1.195$ g cm^{-3}, Cu $K\alpha$, $\lambda = 1.54178$ Å, $\mu = 16.69$ cm^{-1}, $F(000) = 912$, $T = 293$ K, final $R = 0.053$, $wR = 0.060$ for 4031 reflections with $I > 3\sigma(I)$. (IV): [4β,6α(*E*)]-(±)-6-{2-[2-(4-Fluoro-3-methylphenyl)-4,4,6,6-tetramethyl-1-cyclohexen-1-yl]ethenyl}-4-hydroxytetrahydropyran-2-one, $C_{24}H_{31}FO_3$, $M_r = 386.51$, triclinic, $P\bar{1}$, $a = 6.054\,(2)$, $b = 12.931\,(2)$, $c = 14.838\,(3)$ Å, $\alpha = 67.70\,(2)$, $\beta = 85.75\,(2)$, $\gamma = 82.85\,(2)°$, $V = 1066.0\,(8)$ Å^3, $Z = 2$, $D_x = 1.203$ g cm^{-3}, Cu $K\alpha$, $\lambda = 1.54178$ Å, $\mu = 6.86$ cm^{-1}, $F(000) = 414$, $T = 293$ K, final $R = 0.073$, $wR = 0.081$ for 1588 reflections with $I > 3\sigma(I)$. (III) is a potent HMG-CoA reductase inhibitor and has the potential to function as a superior hypocholesterolemic agent; (IV) lacks this activity. (III) and (IV) have different conformations and molecular-model calculations suggest that crystal-packing effects are primarily responsible for

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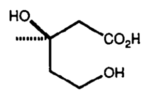
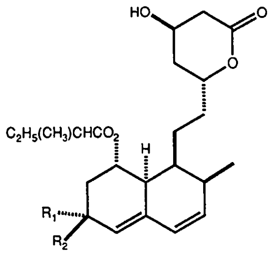
the overall conformation of (IV). The principal intermolecular contacts are hydrogen bonds of the type $\mathrm{O{-}H\cdots O{=}C}$.

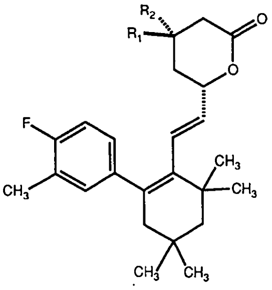
Introduction. Hypercholesterolemia, a condition described by high levels of blood cholesterol, is a major factor in the development of atherosclerosis and related heart problems (Endo, 1985). More than half of the cholesterol in humans is derived from *de novo* synthesis (Grundy, 1978). The rate-limiting step in the biosynthesis of cholesterol is the reduction of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) to mevalonic acid (I), a reaction which is regulated by the enzyme HMG-CoA reductase, (Slakey, Craig, Beytia, Briedis, Feldbrugge, Dugan, Qureshi, Subbarayan & Porter, 1972). The potent natural product inhibitors, mevinolin [(II*a*); Alberts, Chen, Kuron, Hunt, Huff, Hoffman, Rothrock, Lopez, Joshua, Harris, Patchett, Monaghan, Currie, Stapley, Albers-Schonberg, Hensens, Hirshfield, Hoogsteen, Liesch & Springer, 1980] and compactin [(II*b*); Endo, Kuroda & Tsujita, 1976], of HMG-CoA reductase possess the β-hydroxy-δ-lactone-ethylenic moiety and it is known that the active forms of mevinolin and compactin are the corresponding open-chain dihydroxy acids. The synthesis of mevinic acids (compounds that possess the β-hydroxy-lactone-ethylenic fragment) (Rosen & Heathcock, 1986) with enhanced hypocholesterolemic activity, tissue selectivity and decreased side effects remains an active area of pharmaceutical research.



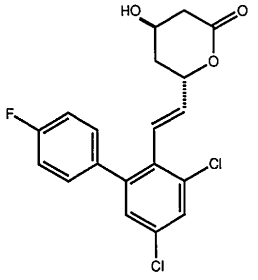
(I)



(IIa): $R_1 = CH_3$, $R_2 = H$
(IIb): $R_1 = R_2 = H$
(IIc): $R_1 = H$, $R_2 = OH$



(III): $R_1 = OH$, $R_2 = H$
(IV): $R_1 = H$, $R_2 = OH$



(V)

Preclinical and clinical studies have shown that RG-12561 [(III); [4α,6β(*E*)]-(±)-6-{2-[2-(4-fluoro-3-methylphenyl)-4,4,6,6-tetramethyl-1-cyclohexen-1-yl]ethenyl}-4-hydroxytetrahydropyran-2-one] is a potent HMG-CoA reductase inhibitor and has the potential to function as a superior hypocholesterolemic agent (Neuenschwander, Regan & Kosmider, 1990). In this paper, we report the crystal structure of the racemic form of (III) and of the racemic 4β,6α-stereoisomer (IV), which lacks hypocholesterolemic activity.

Experimental. Crystallographic data for the two structures are given in Table 1.* Enraf–Nonius CAD-4 diffractometer, incident-beam graphite monochromator. Cell parameters and crystal orientation from 25 automatically centered reflections. $2\theta-\theta$ scans over θ range $1.5(\omega + 0.14\tan\theta)°$. Sets of standard reflection intensities collected every 1 h of X-ray exposure; corrections for variations not made. (III): Diffractometer controlled by *NRCCAD* program (LePage, White & Gabe, 1986); variable step scan with on-line reflection profile processing. (IV): Diffractometer controlled by standard Enraf–Nonius programs (Version 5.0); each scan recorded in 96 steps and subsequently processed off-line with a modified Lehmann–Larsen procedure (Lehmann & Larsen, 1974; Ammon, 1986). All crystallographic calculations performed with the *TEXSAN* (Molecular Structure Corporation, 1989) program system on a DEC MicroVAX II computer; structures solved with the *MITHRIL* (Gilmore, 1983) direct-methods link incorporated in *TEXSAN*. Full-matrix least-squares refinement, atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, pp. 155–175); anisotropic temperature factors for C, O, F and Cl; majority of H atoms were positioned from the C-atom framework; hydroxyl hydrogens placed to optimize intermolecular hydrogen bonding; positional parameters for H kept constant in the case of (III), but varied for all but H3, H3*A*, H4*B* and H24*C* in the case of (IV), individual isotropic temperature factors for H atoms varied except for methyl H atoms for (III); extra density in (III) assumed to be crystallization solvent and modelled as two disordered and overlapping H_2CCl_2 molecules, 0.5 occupancies assigned to each of the four Cl sites and kept constant; $\sum w(F_o - F_c)^2$ minimized, $w = 1/\sigma^2(F_o)$, reflections with $I < 3\sigma(I)$ excluded from refinement. *DIFABS* (Walker & Stuart, 1983) absorption corrections made following full isotropic refinements of structures. Atomic coordinates are listed in Table 2. The *PLOTMD* program

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* Lists of structure factors, anisotropic temperature factors and H-atom coordinates have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54625 (76 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: CR0324]

Table 1. *Crystallographic data for* (III) *and* (IV)

	(III)	(IV)
Solvent for recrystallization	Methylene chloride–hexane	Ethyl acetate–hexane
Crystal dimensions (mm)	0.1 × 0.2 × 0.5	0.033 × 0.1 × 0.3
Molecular formula	$2C_{24}H_{31}FO_3.CH_2Cl_2$	$C_{24}H_{31}FO_3$
Formula weight	857.94	386.51
Crystal system, space group	Triclinic, $P\bar{1}$	Triclinic, $P\bar{1}$
θ range for cell determination (°)	14.0–23.0	6.1–20.5
Lattice parameters		
a (Å)	11.7413 (5)	6.054 (2)
b (Å)	13.0279 (5)	12.931 (2)
c (Å)	16.2332 (9)	14.838 (3)
α (°)	99.456 (4)	67.70 (2)
β (°)	94.217 (4)	85.75 (2)
γ (°)	101.893 (4)	82.85 (2)
Volume (Å^3)	2381.9 (4)	1066.0 (8)
D_x (g cm^{-3})	1.196	1.204
$F(000)$	916	416
μ(Cu $K\alpha$) (cm^{-1})	16.61	6.42
Temperature (K)	293	293
$2\theta_{max}$ (°)	117.9	110.0
No. of standard reflections	7	5
Min., max., av. standard variation in I (%)	−0.8, 2.9, 0.9	−1.3, 1.7, 0.6
Reflection width (w) (°)	0.8	1.0
θ scan speed (° min^{-1})	16.48	0.82–4.12
No. of data measured	7312	3071
No. of unique data	6847	2622
R_{sym} (on F^2)	0.021 for 353 data	0.017 for 294 data
No. of data with $I > 3\sigma(I)$	4031	1588
Min. and max. value of h, k, l	−13, 12; −14, 14; 0, 17	−6, 6; −13, 13; 0, 15
Min., max., av. absorption correction	0.73, 1.12, 0.97	0.56, 1.59, 0.99
Residuals (R, wR)	0.053, 0.060	0.073, 0.081
Goodness of fit (S)	1.79	2.70
Max. Δ/σ	0.12	0.23
Max., min. in final $\Delta\rho$ (e Å^{-3})	0.27, −0.22	0.28, −0.29

Table 2. *Fractional coordinates and equivalent isotropic temperature factors with e.s.d.'s in parentheses for* (III) *and* (IV)

$$B_{eq} = (8\pi^2/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

Table 2 (*cont.*)

	x	y	z	B_{eq} (Å^2)
Compound (III)				
F′	−0.0379 (3)	0.6470 (4)	0.1364 (2)	13.8 (2)
O1′	0.4959 (2)	0.6941 (2)	0.4170 (2)	4.3 (1)
O2′	0.5548 (2)	0.6274 (2)	0.5228 (2)	5.6 (1)
O3′	0.2700 (3)	0.7523 (3)	0.5165 (2)	6.0 (1)
C1′	0.4723 (3)	0.6430 (3)	0.4807 (3)	4.3 (2)
C2′	0.3478 (4)	0.5988 (4)	0.4931 (3)	5.5 (2)
C3′	0.2604 (3)	0.6557 (4)	0.4595 (3)	4.8 (2)
C4′	0.2867 (3)	0.6753 (3)	0.3729 (3)	4.3 (2)
C5′	0.4096 (3)	0.7424 (3)	0.3769 (2)	3.7 (2)
C6′	0.4469 (3)	0.7566 (3)	0.2933 (2)	3.9 (2)
C7′	0.4777 (3)	0.8500 (3)	0.2706 (2)	3.8 (2)
C8′	0.5097 (3)	0.8639 (3)	0.1856 (2)	3.5 (2)
C9′	0.4342 (3)	0.8198 (3)	0.1166 (2)	3.6 (2)
C10′	0.4671 (4)	0.8219 (3)	0.0290 (3)	4.4 (2)
C11′	0.5983 (3)	0.8447 (3)	0.0238 (3)	4.6 (2)
C12′	0.6544 (3)	0.9409 (4)	0.0922 (3)	4.6 (2)
C13′	0.6306 (3)	0.9330 (3)	0.1832 (3)	4.4 (2)
C14′	0.6237 (4)	0.8723 (4)	−0.0620 (3)	6.4 (2)
C15′	0.6452 (4)	0.7455 (4)	0.0328 (3)	6.7 (2)
C16′	0.6353 (4)	1.0469 (4)	0.2299 (3)	6.4 (2)
C17′	0.7245 (4)	0.8907 (5)	0.2282 (3)	7.3 (2)
C18′	0.3089 (3)	0.7706 (3)	0.1222 (2)	4.0 (2)
C19′	0.2357 (4)	0.8357 (4)	0.1525 (3)	4.9 (2)
C20′	0.1181 (4)	0.7971 (5)	0.1582 (3)	6.6 (3)
C21′	0.0784 (5)	0.6902 (7)	0.1328 (4)	8.0 (3)
C22′	0.1440 (6)	0.6218 (5)	0.1027 (4)	7.9 (3)
C23′	0.2621 (4)	0.6633 (4)	0.0970 (3)	5.6 (2)
C24′	0.0384 (4)	0.8659 (6)	0.1911 (4)	11.0 (4)
F″	−0.5299 (3)	0.5185 (2)	0.1375 (2)	9.4 (2)
O1″	0.0000 (2)	0.7025 (2)	0.4079 (2)	4.6 (1)
O2″	0.0991 (2)	0.8652 (2)	0.4516 (2)	5.9 (1)
O3″	−0.2236 (2)	0.7462 (2)	0.5049 (2)	4.8 (1)
C1″	0.0041 (4)	0.8069 (4)	0.4297 (2)	4.1 (2)
C2″	−0.1062 (3)	0.8467 (3)	0.4226 (3)	4.7 (2)
C3″	−0.2176 (3)	0.7642 (3)	0.4213 (3)	4.4 (2)
C4″	−0.2118 (3)	0.6634 (4)	0.3626 (2)	4.6 (2)
C5″	−0.1088 (3)	0.6202 (3)	0.3906 (2)	4.1 (2)
C6″	−0.0878 (3)	0.5319 (3)	0.3270 (2)	4.1 (2)
C7″	−0.0999 (3)	0.4321 (4)	0.3353 (2)	4.1 (2)
C8″	−0.0872 (3)	0.3456 (3)	0.2673 (2)	3.7 (2)
C9″	−0.1538 (3)	0.3254 (3)	0.1931 (2)	3.6 (2)
C10″	−0.1340 (3)	0.2478 (3)	0.1187 (2)	4.3 (2)
C11″	−0.0126 (3)	0.2241 (3)	0.1235 (2)	4.1 (2)
C12″	0.0130 (3)	0.1985 (3)	0.2110 (3)	4.3 (2)
C13″	0.0052 (3)	0.2837 (3)	0.2867 (2)	4.0 (2)
C14″	−0.0111 (4)	0.1270 (4)	0.0568 (3)	6.2 (2)
C15″	0.0766 (4)	0.3190 (4)	0.1069 (3)	5.9 (2)
C16″	−0.0299 (4)	0.2248 (4)	0.3584 (3)	5.4 (2)
C17″	0.1250 (3)	0.3595 (4)	0.3167 (3)	5.6 (2)
C18″	−0.2542 (3)	0.3768 (3)	0.1789 (2)	3.9 (2)
C19″	−0.3489 (4)	0.3632 (3)	0.2249 (3)	4.6 (2)
C20″	−0.4438 (4)	0.4099 (4)	0.2132 (3)	5.0 (2)
C21″	−0.4377 (4)	0.4718 (4)	0.1521 (3)	5.9 (2)
C22″	−0.3476 (5)	0.4879 (4)	0.1046 (3)	6.1 (2)
C23″	−0.2554 (4)	0.4402 (3)	0.1176 (3)	4.8 (2)
C24″	−0.5455 (4)	0.3959 (5)	0.2630 (3)	8.4 (3)
C25	0.7238 (5)	0.9624 (6)	0.6179 (4)	9.1 (3)
Cl1	0.668 (1)	0.897 (1)	0.6865 (7)	21.3 (8)
Cl2	0.6283 (7)	0.9615 (6)	0.5408 (6)	10.6 (3)
Cl3	0.5799 (8)	0.9308 (7)	0.5586 (5)	18.1 (6)
Cl4	0.6778 (5)	0.8883 (6)	0.7079 (4)	8.0 (2)
Compound (IV)				
F	−0.7717 (7)	0.4898 (3)	−0.0899 (3)	7.2 (4)
O1	−0.261 (1)	0.2859 (4)	0.4583 (4)	7.4 (5)
O2	−0.258 (1)	0.3620 (4)	0.5681 (4)	6.9 (5)
O3	0.200 (1)	0.4543 (5)	0.3834 (4)	7.3 (5)
C1	−0.259 (1)	0.3812 (7)	0.4813 (7)	6.8 (8)
C2	−0.203 (2)	0.4825 (6)	0.4000 (6)	5.3 (7)
C3	−0.011 (2)	0.4606 (8)	0.3447 (8)	6.9 (9)
C4	−0.004 (2)	0.3541 (7)	0.3263 (9)	6.2 (9)
C5	−0.215 (1)	0.3027 (6)	0.3556 (5)	4.7 (6)
C6	−0.194 (1)	0.1899 (6)	0.3491 (5)	5.6 (6)
C7	−0.298 (1)	0.1711 (6)	0.2814 (5)	4.6 (6)
C8	−0.293 (1)	0.0683 (5)	0.2600 (4)	3.6 (5)
C9	−0.386 (1)	0.0823 (5)	0.1742 (4)	3.3 (5)
C10	−0.390 (1)	−0.0132 (6)	0.1400 (6)	4.0 (6)
C11	−0.234 (1)	−0.1169 (5)	0.1889 (5)	3.9 (5)
C12	−0.243 (1)	−0.1398 (6)	0.2979 (5)	4.3 (6)
C13	−0.197 (1)	−0.0448 (5)	0.3298 (4)	3.4 (5)
C14	−0.314 (2)	−0.2169 (7)	0.1731 (9)	6.5 (9)
C15	−0.002 (2)	−0.0981 (9)	0.1438 (7)	6.0 (8)
C16	−0.306 (2)	−0.0732 (8)	0.4322 (6)	5.4 (7)
C17	0.058 (1)	−0.0455 (7)	0.3377 (7)	4.7 (7)
C18	−0.490 (1)	0.1909 (5)	0.1077 (4)	3.1 (5)
C19	−0.372 (1)	0.2548 (6)	0.0266 (5)	3.8 (6)
C20	−0.460 (1)	0.3569 (5)	−0.0416 (5)	4.1 (6)
C21	−0.674 (1)	0.3899 (5)	−0.0245 (6)	4.4 (6)
C22	−0.805 (1)	0.3312 (6)	0.0536 (6)	5.2 (7)
C23	−0.709 (1)	0.2297 (6)	0.1188 (6)	4.2 (6)
C24	−0.328 (2)	0.424 (1)	−0.1291 (7)	6.9 (9)

(Luo, Ammon & Gilliland, 1989) was used to display the *ORTEP* drawings (Johnson, 1965) on a VAX-Station II monitor, label the drawings, and prepare print files for a Hewlett–Packard Laser-Jet II printer.

Discussion. Bond lengths, bond angles and selected torsion angles for the two structures are given in Table 3. (III) has two molecules (called III*a* and III*b*) and disordered solvent in the asymmetric unit. We have assumed that the solvent is dichloromethane, and have modeled the density as two overlapping CCl_2 moieties in which the central C atom is common to both molecules. (III*a*) and (III*b*) are enantiomers; the units were chosen to illustrate the formation of an intermolecular hydrogen bond within the asymmetric unit. Figs. 1 and 2 illustrate (III*b*) and (IV), respectively, in orientations that minimize atomic overlap; a separate drawing of

Table 3. *Bond lengths* (Å), *bond angles* (°), *selected torsion angles* (°) *and e.s.d.'s in parentheses for* (III*a*), (III*b*) *and* (IV)

	(III*a*)*	(III*b*)	(IV)
F—C21	1.374 (5)	1.370 (5)	1.379 (7)
O1—C1	1.335 (4)	1.337 (5)	1.401 (8)
O1—C5	1.465 (4)	1.465 (4)	1.466 (8)
O2—C1	1.214 (4)	1.205 (4)	1.216 (8)
O3—C3	1.412 (5)	1.419 (4)	1.423 (9)
C1—C2	1.498 (5)	1.495 (5)	1.46 (1)
C2—C3	1.505 (5)	1.508 (5)	1.43 (1)
C3—C4	1.512 (5)	1.508 (5)	1.50 (1)
C4—C5	1.516 (5)	1.506 (5)	1.47 (1)
C5—C6	1.486 (5)	1.488 (5)	1.486 (9)
C6—C7	1.316 (5)	1.309 (5)	1.338 (8)
C7—C8	1.486 (5)	1.482 (5)	1.476 (8)
C8—C9	1.342 (5)	1.342 (5)	1.371 (7)
C8—C13	1.523 (5)	1.524 (5)	1.510 (8)
C9—C10	1.503 (5)	1.508 (5)	1.505 (8)
C9—C18	1.496 (5)	1.493 (5)	1.470 (8)
C10—C11	1.518 (5)	1.519 (5)	1.508 (9)
C11—C12	1.526 (6)	1.533 (5)	1.529 (9)
C11—C14	1.530 (5)	1.529 (5)	1.540 (9)
C11—C15	1.530 (6)	1.521 (5)	1.52 (1)
C12—C13	1.540 (5)	1.537 (5)	1.537 (9)
C13—C16	1.539 (6)	1.532 (5)	1.54 (1)
C13—C17	1.522 (5)	1.536 (5)	1.552 (9)
C18—C19	1.387 (5)	1.382 (5)	1.380 (9)
C18—C23	1.373 (6)	1.394 (5)	1.383 (9)
C19—C20	1.385 (6)	1.391 (5)	1.394 (9)
C20—C21	1.357 (8)	1.374 (6)	1.351 (9)
C20—C24	1.493 (7)	1.489 (6)	1.50 (1)
C21—C22	1.350 (8)	1.356 (6)	1.37 (1)
C22—C23	1.396 (7)	1.376 (6)	1.39 (1)
C1—O1—C5	121.8 (3)	123.8 (3)	115.4 (6)
O1—C1—O2	117.4 (4)	117.3 (4)	114.4 (8)
O1—C1—C2	119.9 (4)	119.7 (4)	115.4 (7)
O2—C1—C2	122.5 (4)	123.0 (4)	128.4 (7)
C1—C2—C3	114.8 (4)	115.2 (4)	112.0 (8)
O3—C3—C2	107.4 (4)	106.5 (3)	116.6 (8)
O3—C3—C4	111.7 (4)	110.8 (3)	104.3 (8)
C2—C3—C4	109.2 (3)	108.9 (3)	114.8 (8)
C3—C4—C5	110.2 (3)	111.1 (3)	111.9 (8)
O1—C5—C4	111.1 (3)	112.0 (3)	107.9 (7)
O1—C5—C6	106.5 (3)	106.9 (3)	106.9 (6)
C4—C5—C6	113.8 (3)	112.8 (3)	111.0 (7)
C5—C6—C7	123.9 (4)	126.0 (4)	121.7 (7)
C6—C7—C8	123.9 (4)	123.8 (4)	130.3 (7)
C7—C8—C9	121.1 (3)	120.6 (3)	115.5 (6)
C7—C8—C13	115.6 (3)	116.2 (3)	121.7 (5)
C9—C8—C13	123.3 (3)	123.1 (3)	122.7 (5)
C8—C9—C10	122.9 (4)	122.5 (3)	122.4 (6)
C8—C9—C18	121.7 (3)	122.4 (3)	123.2 (5)
C10—C9—C18	115.4 (3)	115.1 (3)	114.3 (5)
C9—C10—C11	113.9 (3)	114.2 (3)	116.3 (6)
C10—C11—C12	107.5 (3)	107.1 (3)	107.5 (6)
C10—C11—C14	109.8 (4)	109.6 (3)	108.8 (6)
C10—C11—C15	109.9 (4)	109.9 (3)	109.1 (7)
C12—C11—C14	109.0 (4)	109.3 (3)	108.9 (7)
C12—C11—C15	112.9 (4)	112.5 (3)	112.9 (6)
C14—C11—C15	107.8 (4)	108.5 (3)	109.5 (8)
C11—C12—C13	117.3 (3)	116.8 (3)	117.9 (6)
C8—C13—C12	110.9 (3)	111.6 (3)	111.2 (5)
C8—C13—C16	108.9 (3)	108.8 (3)	111.4 (6)
C8—C13—C17	110.5 (3)	111.0 (3)	110.3 (6)
C12—C13—C16	107.2 (3)	106.9 (3)	105.1 (6)
C12—C13—C17	111.5 (3)	111.1 (3)	110.2 (6)
C16—C13—C17	107.6 (4)	107.2 (3)	108.6 (7)
C9—C18—C19	119.1 (4)	121.7 (4)	120.1 (7)
C9—C18—C23	122.6 (4)	120.5 (4)	122.5 (6)
C19—C18—C23	118.3 (4)	117.8 (4)	117.3 (7)
C18—C19—C20	122.8 (5)	123.2 (4)	123.6 (8)
C19—C20—C21	115.6 (5)	115.4 (4)	115.4 (7)
C19—C20—C24	123.5 (6)	123.3 (5)	122.4 (9)
C21—C20—C24	121.0 (6)	121.3 (4)	122.2 (8)
F—C21—C20	118.4 (7)	117.6 (5)	118.2 (8)
F—C21—C22	116.6 (7)	118.1 (5)	116.9 (7)
C20—C21—C22	125.1 (5)	124.3 (4)	125.0 (7)
C21—C22—C23	118.0 (5)	118.8 (5)	117.3 (8)
C18—C23—C22	120.2 (5)	120.6 (4)	121.4 (8)
O1—C1—C2—C3	26.7 (6)	21.3 (6)	−47 (1)
O1—C5—C4—C3	−54.2 (4)	−49.5 (5)	−56 (1)
O1—C5—C6—C7	117.1 (4)	123.1 (4)	132.5 (8)
O2—C1—O1—C5	163.2 (3)	171.7 (3)	−167.5 (7)

Table 3 (*cont.*)

	(III*a*)*	(III*b*)	(IV)
O2—C1—C2—C3	−159.0 (4)	−161.6 (4)	117 (1)
O3—C3—C2—C1	76.4 (5)	74.6 (4)	−80 (1)
O3—C3—C4—C5	−59.3 (4)	−57.1 (4)	137.9 (9)
C1—O1—C5—C4	36.0 (5)	25.2 (5)	52.7 (9)
C1—O1—C5—C6	160.4 (3)	149.2 (4)	172.2 (7)
C1—C2—C3—C4	−44.9 (6)	−45.0 (5)	42 (1)
C2—C1—O1—C5	−22.3 (6)	−11.0 (6)	−2 (1)
C2—C3—C4—C5	59.4 (5)	59.7 (5)	9 (1)
C3—C4—C5—C6	−174.3 (3)	−170.2 (4)	−172.3 (9)
C4—C5—C6—C7	−120.2 (4)	−113.3 (5)	−110 (1)
C5—C6—C7—C8	177.0 (3)	174.8 (3)	177.2 (7)
C6—C7—C8—C9	−58.5 (6)	−57.2 (6)	−168.1 (8)
C6—C7—C8—C13	123.1 (4)	122.2 (4)	13 (1)
C7—C8—C9—C10	173.3 (3)	172.3 (3)	178.4 (7)
C7—C8—C9—C18	−10.4 (6)	−8.9 (6)	−1.3 (9)
C7—C8—C13—C12	−179.4 (3)	−178.3 (3)	171.4 (6)
C7—C8—C13—C16	62.8 (4)	63.9 (4)	54.6 (8)
C7—C8—C13—C17	−55.2 (5)	−53.8 (5)	−66.1 (8)
C8—C9—C10—C11	−18.7 (5)	−19.9 (6)	−16 (1)
C8—C9—C18—C19	−67.3 (5)	−60.6 (6)	99.3 (7)
C8—C9—C18—C23	114.1 (5)	119.8 (4)	−85.4 (8)
C8—C13—C12—C11	31.6 (5)	32.2 (5)	37.8 (9)
C9—C8—C13—C12	2.1 (5)	1.0 (5)	−7.1 (9)
C9—C8—C13—C16	−115.7 (4)	−116.7 (4)	−123.9 (7)
C9—C8—C13—C17	126.3 (4)	125.5 (4)	115.4 (7)
C9—C10—C11—C12	47.7 (4)	48.5 (4)	42.4 (9)
C9—C10—C11—C14	166.2 (4)	166.9 (3)	160.2 (8)
C9—C10—C11—C15	−75.5 (5)	−73.9 (4)	−80.3 (9)
C10—C9—C8—C13	−8.3 (6)	−7.1 (6)	−3 (1)
C10—C9—C18—C19	109.3 (4)	118.4 (4)	−80.5 (7)
C10—C9—C18—C23	−69.3 (5)	−61.3 (5)	−94.8 (8)
C10—C11—C12—C13	−56.2 (4)	−56.5 (4)	−55.1 (9)
C11—C10—C9—C18	164.8 (3)	161.2 (3)	163.3 (7)
C11—C12—C13—C16	150.4 (4)	151.1 (3)	158.4 (7)
C11—C12—C13—C17	−92.1 (4)	−92.2 (4)	−84.7 (8)
C13—C8—C9—C18	167.9 (4)	171.8 (3)	177.3 (6)
C13—C12—C11—C14	−175.1 (3)	−175.1 (3)	−172.9 (7)
C13—C12—C11—C15	65.1 (5)	64.3 (5)	65.2 (9)

* The torsion angles listed for (III*a*) were calculated for the mirror image (enantiomer) of the (III*a*) coordinates shown in Table 2.

(III*a*) is not given. The enantiomeric relationship between (III*a*) and (III*b*) can be seen by visualizing a mirror plane of symmetry in the plane of the paper of Fig. 1. The hydroxylactone rings in (III) and (IV) contain two chiral centers, C3 (hydroxy-linked) and C5 (ethylene-linked); the two structures are diastereomers (epimeric alcohols at C3). The stereochemistries of C3 and C5 are: (III*a*) = (*R*,*S*); (III*b*) = (*S*,*R*); (IV) = (*S*,*S*). Fig. 3 illustrates the three molecules in identical orientations with respect to the cyclohexene ring. For this figure, (III*a*) has been replaced by its mirror image (III*a**) to show the similarities between the three structures. The overall conformations of (III*a**) and (III*b*) show small torsion-angle differences at C9—C18 (7.1° average difference in four dihedral angles) and C5—C6 (6.4° average difference in two dihedral angles). Fig. 3 shows that the major conformational differences between (III) and (IV) are associated with the ethylene-bridge, hydroxylactone and fluorobenzene conformations. The average dihedral angles are: C7—C8 in (III) = 57.6, (IV) = 12.4°; C9—C18 in (III) = 64.6, (IV) = 82.9°. The angles suggest different degrees of conjugation between the cyclohexene and ethylene and fluorobenzene groups. In addition, bond lengths in the C6=C7—C8=C9 butadiene fragments reflect differences in the C7—C8 twist and degrees of conjugation: (III) = 1.312–1.484–1.342; (IV) = 1.338–1.476–1.371 Å. The C5—C6 dihedral angles are similar in (III) and (IV), with values for O1—C5—C6—C7 and C4—C5—C6—C7 of 120.1 (av.) and 116.8° (av.) in (III) and 132.5 and −110.0° in (IV).

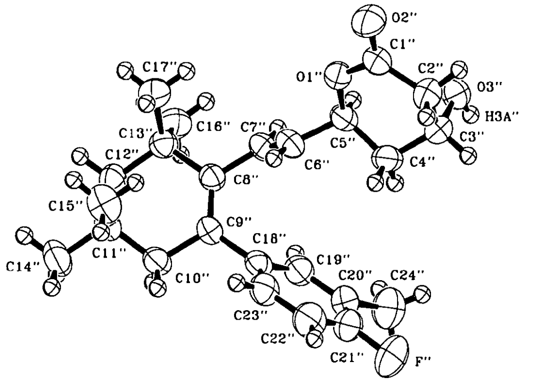


Fig. 1. *ORTEP* drawing of (III*b*). The C, O and F atoms are shown as 50% ellipsoids, and the H atoms are depicted as spheres with $B = 1.5$ Å^2. An *ORTEP* drawing of (III*a*) is not shown; (III*a*) is essentially the mirror image of (III*b*).

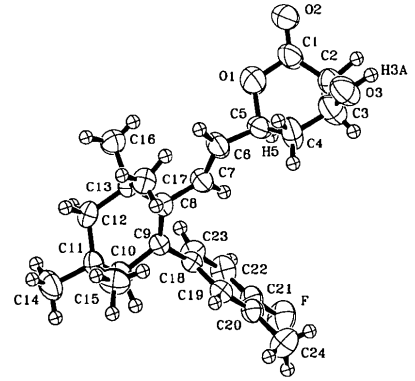
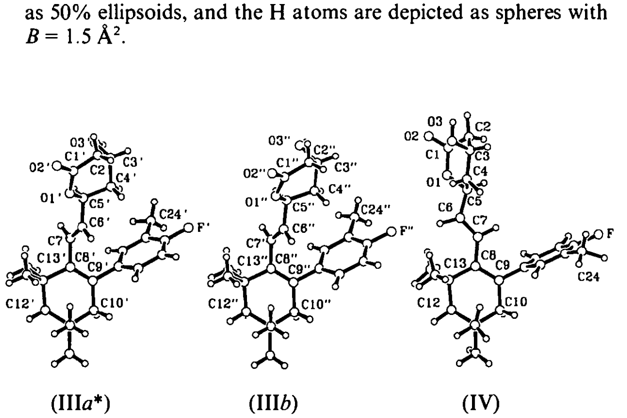


Fig. 2. *ORTEP* drawing of (IV). The C, O and F atoms are shown as 50% ellipsoids, and the H atoms are depicted as spheres with $B = 1.5$ Å^2.



(III*a**) (III*b*) (IV)

Fig. 3. Ball and stick drawings of (III*a**), (III*b*) and (IV). (III*a**) is the enantiomer of (III*a*).

Models of (III) and (IV) were subjected to energy minimization with the *AM*1 procedure (Dewar, Zoebisch, Healy & Stewart, 1985; Stewart & Seiler, 1989), and calculations were performed for a so-called (IV)-like-(III) model, in which the 4-fluoro-3-methylphenyl substituent in (IV) was rotated about the phenyl–cyclohexene bond to place the 3-methyl group below the cyclohexene ring as in (III). The *AM*1-calculated heats of formation for (III), (IV) and (IV)-like-(III) were −38.28, −38.44 and −38.56 kJ mol^{-1}, respectively. The ethylene–cyclohexene and fluoromethylphenyl–cyclohexene conformations in the models of (III) and (IV)-like-(III) were similar to the observed conformations in (III), in which the ethylenic C=C and phenyl moieties are both rotated by substantial margins out of the cyclohexene C=C. For example, the C6—C7—C8—C9 and C8—C9—C18—C19 torsion angles in the models are −63.6, −64.0° in (III) and −74.7, −69.0° in (IV)-like-(III). The average torsion angles observed in (III*a**) and (III*b*) are −57.7, −63.9°, compared with −168.1, 99.3° in (IV). These torsion angles in the *AM*1-(IV) model were −103.6, 55.5°. These results suggest that the small C7—C8 twist (*ca* 12°) and large C9—C18 twist (*ca* 81°) observed in the crystal structure of (IV) arise primarily from crystal-packing effects.

A search of the Cambridge Structural Database (1990, July 1990 update) for the hydroxylactone fragment in (III) and (IV) located four structures: (II*a*) (Sato, Hata, Tsujita, Terahara & Tamura, 1984); (II*b*) (Brown, Smale, King, Hasenkamp & Thompson, 1976); (II*c*) (Haruyama, Kuwano, Kinoshita, Terahara, Nishigaki & Tamura, 1986); (V) (Stokker, Alberts, Anderson, Cragoe, Deana, Gilfillan, Hirshfield, Holtz, Hoffman, Huff, Lee, Novello, Prugh, Rooney, Smith & Willard, 1986). (V) was very similar to (III) and (IV). The central ring in (V) is dichlorobenzene *versus* tetramethylcyclohexene in (III) and (IV), and the fluorobenzene ring in (V) lacks the methyl substituent found in (III) and (IV). The configurations at C3 and C5 in (V) are opposite to each other (*R*,*S*) as in (III). The average torsion angles about C7—C8 of 57.5 and C9—C18 of 54.7° in (V) are similar to the corresponding values of 57.6 and 64.6° in (III).

Data on intermolecular distances are listed in Table 4. Crystal-packing drawings are shown in Figs. 4 and 5; in both (III) and (IV), the shortest intermolecular distances involve the hydroxylactone rings and are of the O—H···O=C type. In (III), there is an extended system of O—H···O=C hydrogen bonds parallel to the *a* axis. Fig. 4 illustrates that (III*b*) is a donor to its asymmetric unit mate (III*a*), and an acceptor for a second (III*a*) at $1 + x, y, z$. This hydrogen-bonded string and its symmetry analog through $\frac{1}{2},0,\frac{1}{2}$ create a tunnel along [100] containing the dichloromethane molecules. The distances between the atoms of the solvate and (III) are all larger than the associated van der Waals radii. In (IV), two molecules on opposite sides of a center of symmetry are involved in the formation of a hydrogen-bonded dimer (Fig. 5). Each molecule is both donor and acceptor to a center-of-symmetry related mate. This arrangement localizes the polar interactions to one region of the unit cell and leaves the remaining hydrophobic portion of the molecule to interact with similar regions of its neighbors.

Table 4. *Hydrogen-bond parameters and shortest distances with chlorine atoms* (Å)

	A—H···*B*	*A*—H	H···*B*	*A*···*B*
(IV)	O3—H3*A*···O2^{i}	0.96	1.84	2.798 (7)
(III)	O3′—H3*A*′···O2″	0.96	1.99	2.953 (4)
	O3″—H3*A*″···O2′^{ii}	0.96	1.85	2.801 (4)

	O···Cl		O···Cl
O1′···Cl3	3.442 (8)	O3″···Cl1^{ii}	3.73 (1)
O1′···Cl2	3.687 (9)	Cl2···Cl3^{iii}	3.482 (5)
O2″···Cl2^{iii}	3.497 (8)	Cl3···Cl3^{iii}	3.52 (2)
O3″···Cl2^{ii}	3.585 (9)		
O3″···Cl3^{ii}	3.71 (1)		

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

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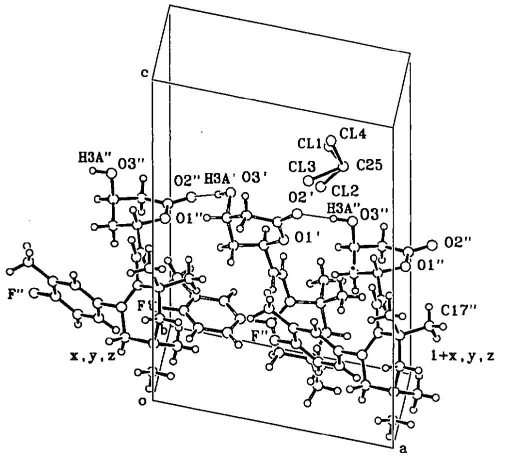

Fig. 4. Packing diagram for (III) viewed approximately along the *b* axis. The C25–Cl1–Cl2–Cl3–Cl4 moiety represents the disordered solvent complex.

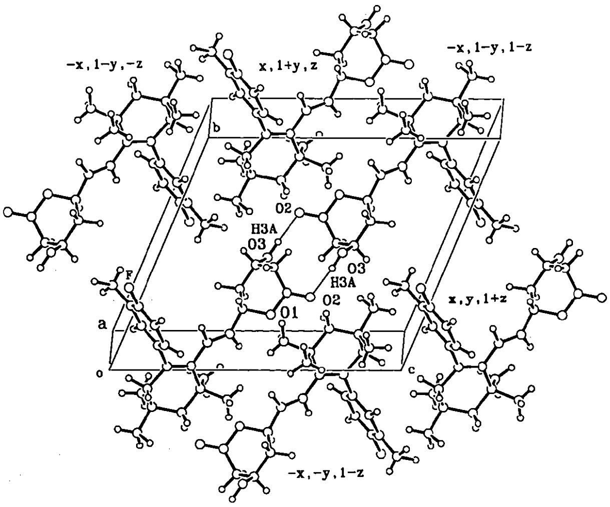

Fig. 5. Packing diagram for (IV).

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Tris(2-imidazolyl)phosphine Hemihydrate

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Abstract. $C_9H_9N_6P.\frac{1}{2}H_2O$, $M_r = 241.2$, monoclinic, $C2/c$, $a = 13.822$ (4), $b = 8.0133$ (8), $c = 21.843$ (3) Å, $\beta = 105.41$ (2)°, $V = 2332.4$ (9) Å^3, $Z = 8$, $D_m = 1.37$ (2), $D_x = 1.374$ Mg m^{-3}, $\lambda(\mathrm{Cu}\ K\alpha) = 1.540598$ Å, $\mu = 2.00$ mm^{-1}, $F(000) = 1000$, $T = 295$ (1) K, $R = 0.0904$, $wR = 0.0662$ for 1724 unique reflections and 180 parameters. Bond lengths and angles are close to normal but the PC—NH distances [average 1.323, range 1.316 (5)–1.329 (5) Å] are shorter than the PC—N distances [average 1.341, range 1.333 (5)–1.342 (5) Å]. The conformation of the molecule is determined by the water molecule which hydrogen bonds pairs of phosphine molecules together.

Introduction. Early attempts by us to produce the title compound by the literature method (Curtis & Brown, 1980) gave instead bis(2-imidazolyl)phosphinic acid (Howard-Lock, Lock, Penny & Turner, 1989). By coincidence the only common published data for the two compounds, namely the NMR spectra and melting points, were the same. Discussions with R. S. Brown revealed that the published general preparative procedure had to be modified for the title compound.† To fully characterize the title compound we have determined its structure. Colourless crystals were grown from methanol solution.

Experimental. Density by suspension in a dichloromethane–chloroform mixture. Crystal chosen for diffraction: plate 0.08 × 0.15 × 0.42 mm. Unit-cell parameters refined by least-squares fit of positional parameters for 20 reflections, $50.2 < 2\theta < 76.5°$, on a Rigaku AFC6R rotating-anode diffractometer, running at 50 kV and 50 mA with the use of graphite-monochromated Cu $K\alpha$ radiation ($\lambda = 1.540598$ Å at 295 K). Intensities $0 \le h \le 16$, $0 \le k \le 9$, $-25 \le l \le 25$ ($2\theta_{\max} = 120°$) measured by an ω–2θ scan technique at a scan rate of 32.0° min^{-1} in 2θ. Total background time to scan ratio was 1:1. Methods of treating intensities have been described (Hughes, Krishnamachari, Lock, Powell & Turner, 1977; Lippert, Lock, Rosenberg & Zvagulis, 1977). Three standard reflections collected every 150 reflections ($3\bar{1}\bar{1}$, $R_{\mathrm{merge}} = 0.030$; $40\bar{2}$, 0.036; $1\bar{1}4$, 0.033) showed no instrument instability or crystal decay. 1959 reflections measured, zonal reflections averaged to give 1724 independent reflections, $R_{\mathrm{int}} = 0.0307$. Reflections with $3\sigma_I \ge I \ge -3\sigma_I$ (708) treated by the method of French & Wilson (1978). Lp corrections were made, as was a correction for absorption by the empirical method (North, Phillips & Mathews, 1968) (absorption correction factors $1.144 \le A^* \le 1.706$). Structure solved by direct methods based on 247 reflections with $|E| > 1.2$ and 50 sets of starting phases (Gilmore, 1984). H atoms located from difference map. Anisotropic full-matrix least-squares refinement minimized $\sum w(|F_o| - |F_c|)^2$, $w = (\sigma_F{}^2 + 0.0005F_o^2)^{-1}$. Scale, positional parameters for all atoms, anisotropic temperature factors for non-H atoms varied, 180 parameters. H atoms refined with fixed temperature factors. Final $R = 0.0904$, $wR = 0.0662$, $S = 1.031$. The large value of R is caused by the number of reflections with $I < 3\sigma_I$. Refinement ended when $(\Delta/\sigma)_{\max} = 0.004$. Final difference map

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† Lists of structure factors, anisotropic thermal parameters, intramolecular bond lengths and angles involving H atoms, best planes and dihedral angles and a description of the preparative procedure have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54509 (16 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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