where C(9)—O(1) is 1·362 (3) Å and O(3)—C(4) is 1·431 (5) Å, although the difference between the bond lengths O(1)—C(2) 1·434 (5) Å, and C(2)—O(3) 1·377 (5) Å in (II) is much more pronounced than the corresponding marginal difference in the title compound in which the torsion angle O(1)—C(2)—O(3)—C(4) of 69·1 (4)° in (II) is not different from that in (I). The aromatic rings of molecules at (x, y, z) and $(x, 1+y, z)$ form stacks, the overlap between molecules in these stacks being illustrated in Fig. 2. The average perpendicular distance between the C atoms in the aromatic ring and the plane through these related atoms in adjacent molecules is 3·566 (7) Å, which is close to the corresponding distances of 3·472 (96) and 3·503 (96) Å found in (II).

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The Tri-ortho-thymotide–3-Buten-2-ol (2/1) Clathrate at 153 K. Lattice Energy and Chiral Discrimination

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Abstract. 1,7,13-Trimethyl-4,10,16-tris(1-methylethyl)-6H,12H,18H-tribenzo[b,f,j][1,5,9]trioxacyclododecin-6,12,18-trione-3-buten-2-ol (2/1), $C_{33}H_{36}O_6 . \frac{1}{2}C_4H_8O$, $M_r = 564·70$, trigonal, $P3_121$, $a = 13·444$ (3), $c = 30·217$ (9) Å, $V = 4730$ (1) Å³, $Z = 6$, $D_x = 1·190$ g cm⁻³, $\lambda(Mo\,K\alpha) = 0·71069$ Å, $\mu = 0·875$ cm⁻¹, $F(000) = 1812$, $T = 153$ K, $R = 0·068$ for 1657 observed reflections at the $|F_o| > 3\sigma(F_o)$ level. The host structure was refined starting from previously determined coordinates in an isomorphous tri-o-thymotide (TOT) clathrate. A strained conformation of the guest, derived from a calculated two-dimensional energy map, was favourably used as rigid component in the X-ray model. Evidence for low chiral discrimination of the guest was quantitatively demonstrated.

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Correlation of configuration between TOT in a single crystal and the major included enantiomer was shown to obey previously established structural rules. Lattice-energy calculations corroborate the experimental observations.

Introduction. Strongly basic reagents are required to promote the ring-opening of epoxides involving a rearrangement to allylic alcohols (e.g. Price & Carmelite, 1966). Pseudo-enzymatic activity of TOT clathrate cages was demonstrated by the occurrence of the analogous chemical transformation of simple enclathrated epoxides, but under acidic conditions (Gerdil & Barchietto, 1987). A noteworthy result is the acid-catalysed rearrangement of included cis-2,3-dimethyloxirane (1) to form quantitatively 3-buten-2-ol (2) in slight enantiomeric excess, when clathrate crystals of TOT/(1) are submitted to a flow of gaseous HCl or HBr. The present structure analysis is part of a

general study of the stereochemical factors controlling the chemical path of the acid-catalysed allylic rearrangement of epoxides in the solid state.

Experimental. Colourless single crystal of average dimensions $0.31 \times 0.26 \times 0.26$ mm sealed inside a Lindemann-glass capillary; Philips PW 1100 diffractometer, graphite-monochromated Mo $K\alpha$ ($\lambda = 0.71069$ Å); lattice parameters from 22 reflections ($7.8 < \theta < 10.3°$). Data collection: 5726 reflections consisting of Friedel pairs within $6 < 2\theta < 48°$ ($0 < h < 15$, $0 < k < 15$, $0 < l < 34$), ω–2θ scans, ω-scan angle $1.20°$, scan speed $2.4°$ min^{-1}; two standard reflections (522 and 309) monitored at 90 min intervals (no significant intensity variations); Lorentz–polarization correction (no absorption or extinction correction). After merging, 2807 unique reflections with $R_{int} = 0.033$, 1657 considered observed with $|F_o| > 3\sigma(F_o)$.

Non-H atoms of host structure isotropically refined (H atoms included but not refined), starting from the coordinates taken from an isomorphous TOT clathrate (Allemand & Gerdil, 1981); $R = 0.140$. ΔF syntheses revealed three major unique peaks within the region of the cage. Starting with a minimum-energy geometry calculated by the force-field method (*MM2*: Allinger, 1977), various guest conformations were successively tested as rigid bodies in the crystallographic model (see *Discussion*). Final TOT structure refined anisotropically by full-matrix least squares using unit weights for the $|F|$ values; positions of the H atoms calculated, but not refined, and included in the model with isotropic temperature factor 0.078 Å^2; rigid-body guests with overall temperature factor and equal weight of $1/4$ for both enantiomers. $R = 0.068$, $wR = 0.071$, $S = 2.56$; max. and ave. $|\Delta|/\sigma$ values for non-H atomic parameters 0.04 and 0.01; max. and min. heights in the final ΔF synthesis are ± 1.2 e Å^{-3}. Scattering factors for C and O from Cromer & Mann (1968), for H atoms from Stewart, Davidson & Simpson (1965). The data reduction was processed by a local version of *XRAY76* (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976). The refinements were carried out by the *XTAL*2.4 system (Stewart & Hall, 1984).

Discussion. The final atomic parameters are given in Table 1* and the atom-numbering scheme is depicted in Fig. 1.

Disordered host structure. During the early stage of the host refinement, ΔF syntheses revealed a peak (1.4 e Å^{-3}) near the carbonyl oxygen O(133), the

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Table 1. *Atomic coordinates* ($\times 10^4$) *and equivalent isotropic thermal parameters* (Å^2 $\times 10^3$)

$$U_{eq} = \tfrac{1}{3}\sum_i\sum_j U_{ij}a_i a_j (\mathbf{a}_i\mathbf{a}_j).$$

TOT	x	y	z	U_{eq}
O(1)	3327 (5)	9830 (5)	1056 (2)	34 (3)
O(2)	4658 (5)	8807 (5)	933 (2)	30 (3)
O(3)	3387 (5)	8150 (5)	1712 (2)	27 (3)
O(11)	2043 (6)	8948 (6)	503 (2)	44 (4)
O(22)	3823 (7)	7161 (6)	546 (2)	51 (4)
O(133)	1889 (20)	7018 (23)	1278 (7)	41 (11)
O(233)	1591 (24)	6836 (26)	1494 (11)	57 (14)
C(1)	2016 (8)	8742 (8)	1632 (3)	29 (4)
C(2)	2488 (8)	9704 (8)	1371 (3)	30 (4)
C(3)	2237 (8)	10594 (8)	1423 (4)	40 (5)
C(4)	1503 (9)	10456 (9)	1766 (4)	39 (5)
C(5)	1028 (9)	9501 (9)	2035 (4)	44 (6)
C(6)	1262 (7)	8604 (8)	1974 (3)	29 (4)
C(7)	706 (9)	7546 (9)	2268 (4)	46 (5)
C(8)	2720 (9)	11617 (9)	1109 (4)	41 (5)
C(9)	3227 (10)	12746 (10)	1370 (5)	57 (6)
C(10)	1789 (11)	11516 (10)	787 (5)	61 (7)
C(11)	3019 (10)	9425 (8)	643 (4)	40 (5)
C(12)	4086 (8)	9730 (8)	376 (3)	31 (4)
C(13)	4880 (8)	9431 (8)	525 (3)	32 (5)
C(14)	5928 (9)	9800 (8)	327 (3)	33 (5)
C(15)	6154 (8)	10459 (9)	−57 (4)	38 (5)
C(16)	5364 (9)	10744 (8)	−216 (3)	39 (5)
C(17)	4320 (9)	10393 (8)	−6 (3)	33 (5)
C(18)	3498 (9)	10765 (9)	−183 (3)	42 (6)
C(19)	6801 (9)	9507 (10)	507 (4)	44 (6)
C(20)	7932 (10)	10621 (11)	633 (5)	71 (7)
C(21)	7081 (12)	8824 (13)	185 (4)	70 (8)
C(22)	4164 (8)	7639 (7)	894 (4)	31 (4)
C(23)	4147 (7)	7098 (8)	1323 (3)	27 (4)
C(24)	3747 (8)	7321 (8)	1715 (3)	31 (4)
C(25)	3698 (7)	6794 (8)	2121 (3)	32 (4)
C(26)	4103 (8)	6019 (9)	2119 (4)	38 (5)
C(27)	4513 (8)	5787 (8)	1725 (3)	33 (5)
C(28)	4531 (8)	6298 (8)	1326 (3)	31 (4)
C(29)	5025 (10)	6018 (9)	929 (4)	44 (6)
C(30)	3268 (9)	7065 (9)	2542 (4)	39 (5)
C(31)	4267 (10)	7729 (10)	2869 (4)	50 (6)
C(32)	2290 (9)	5973 (10)	2742 (4)	52 (6)
C(33)	2335 (9)	7817 (9)	1550 (4)	43 (5)

Guest molecule 3-buten-2-ol
R configuration

O(38)	−80	2122	1726	81 (5)*
C(34)	−1419	2744	1904	
C(35)	−151	3113	1830	
C(36)	390	4015	1471	
C(37)	1440	4377	1306	
H(134)	−1801	2084	2172	
H(234)	−1521	3486	2005	
H(334)	−1934	2365	1598	
H(35)	335	3480	2143	
H(36)	−116	4393	1343	
H(137)	1799	5040	1046	
H(237)	1980	4031	1426	
H(38)	698	2319	1711	

S configuration

O(38)	−388	2092	1528	81 (5)*
C(34)	1424	2791	1948	
C(35)	−581	3032	1565	
C(36)	532	4150	1626	
C(37)	1457	4489	1369	
H(134)	−2241	1968	1894	
H(234)	−1644	3484	1979	
H(334)	1053	2724	2268	
H(35)	−985	3086	1248	
H(36)	575	4716	1899	
H(137)	2250	5315	1427	
H(237)	1456	3960	1091	
H(38)	59	2185	1275	

Origin at 3,21. Occupancy for O(133) and O(233) is 0.55 and 0.45, respectively.

* Overall isotropic factor.

thermal parameter of which showed a large magnitude of 0·14 Å² and a high shift-to-e.s.d. ratio of 5·0. Unusually large thermal parameters for O(33) were also observed in other isostructural TOT clathrates. This was interpreted as a two-positional disorder of the carbonyl oxygen; accordingly, the positions and constrained occupancy factors for O(133) and O(233) were refined at later stages of the analysis.

The final ΔF map showed a few residual peaks and minima of significant magnitude, located in the vicinity of some of the TOT non-H atoms. These residual densities, which varied between $\pm 1\cdot2$ e Å⁻³, appeared to be independent of the tested guest conformations. Consequently, two-positional contributions were assigned to certain atoms of the host molecule as described above for O(33). No significant improvement resulted from this approach as demonstrated by further ΔF syntheses. The residual electron density unaccounted for by our model is tentatively interpreted as resulting, at least partly, from unpredictable conformational distortions of the host molecule (and/or from local disorders of the host lattice) engendered by partial occupancy of the cages. Indeed, the occurrence of vacant cavities has been systematically observed in TOT cage clathrates (Gerdil, 1987). This was again confirmed by NMR measurements on the title compound, that revealed occupancy factors ranging from 0·67 to 0·73 in single crystals selected at random.

Guest conformation. ΔF syntheses revealed three major peaks within the region of the cage (see Fig. 2).
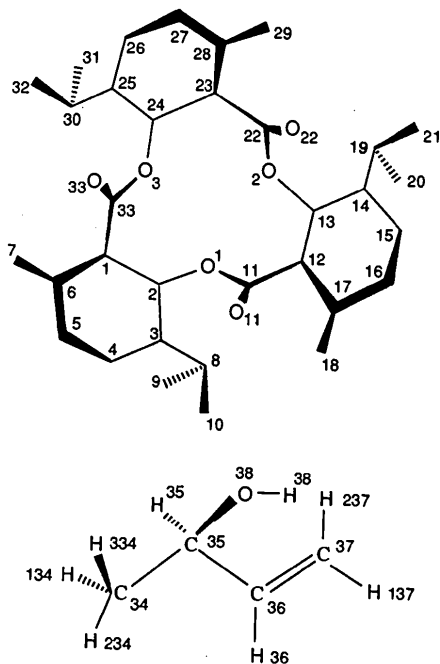
The peak located on the crystallographic twofold axis was initially attributed to the hydroxyl O atom. The two major peaks on each side of the twofold axis were attributed to the overlap of the terminal ethylenic CH_2 group of the guest, in one of two symmetry-related positions, with the CH_3 group of the equivalent molecule rotated by 180°. A similar weighted contribution from the other enantiomer amplifies the local peak smearing. For lack of unequivocal crystallographic information on the guest conformation, a two-dimensional strain-energy map was calculated for the molecule as a function of the dihedral angles $\tau_1 = C(36)-C(35)-O(38)-H(38)$ and $\tau_2 = C(34)-C(35)-C(36)-C(37)$, all other relevant structural parameters being relaxed for each pair of values τ_1, τ_2 (*MM2* program: Allinger, 1977). The global minimum energy conformer $(E_s = 10\cdot33$ kJ mol⁻¹; $\tau_1 = 55\cdot8$, $\tau_2 = 119\cdot8°)$ was initially used as rigid body in the X-ray model, but proved unsatisfactory owing to the occurrence of prohibitively short contacts between the terminal ethylenic H atoms and the carbonyl oxygens (final $R = 0\cdot080$).

An empirical fit of the atoms O(38), C(34) and C(37) of the guest with the major peaks of the ΔF synthesis by varying τ_2 proved more rewarding. A requisite was that the non-bonded distances $O(38)\cdots C(34)$ and $O(38)\cdots C(37)$ should be approximately equal. Several
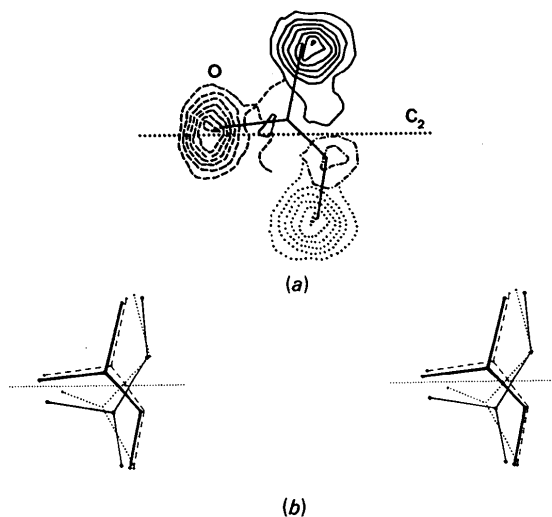

(a)

(b)

Fig. 2. (a) Compound view of difference maps plotted on planes perpendicular to c within the cage area; lowest contour at 0·30 e Å⁻³, contour interval 0·30 e Å⁻³. Solid, dashed, chain-dotted and dotted lines at $z \simeq 0\cdot20$, 0·17, 0·16 and 0·14, respectively. The upper and lower planes are symmetry-related by the crystallographic C_2 axis. The final unique orientation of the (R)-(2) framework is shown in projection. (b) Stereoviews, down the c axis, of the calculated positions for (R)-(2) (dashed) and (S)-(2) (dotted) compared with their corresponding orientation in the X-ray model (thick and thin line, respectively). For clarity, only a unique position is shown for each molecule.

Fig. 1. Idealized view of (M)-(−)-tri-o-thymotide together with the guest molecule, and atom numbering in the structure analysis.

conformations were empirically tested for different values of τ_2. The structure that yielded the lowest R (0·068) is characterized by a strain energy of $E_s = 13·7$ kJ mol^{-1} ($\tau_1 = 62·7$, $\tau_2 = -171·6°$). This conformation lies in the vicinity of a saddle point of the energy map, on the lowest-energy path between the global and a vicinal local energy minimum at $E_s = 11·8$ kJ mol^{-1}. The τ_1 values suffer only minor variations along this path. However, the conformer associated with this local minimum (second in importance) shows an unacceptably short C(34)···C(37) distance and increases R to 0·078 when used in the X-ray model. Hence, a distortion of the guest framework favours its inclusion, as demonstrated below by packing-energy calculations.

Packing-energy analysis. Minimization of the clathrate lattice energy including the X-ray guest model was performed by means of the *PCK*6 program (Williams, 1972*b*, 1974). The function for non-bonded interatomic potential energy $E(r) = -Ar^{-6} + B\exp(-Cr)$ was applied. The coefficients A, B and C for C···C, C···H and H···H interactions were taken from Williams (1972*a*); those for O···O, O···H and O···C from Gavezzotti & Simonetta (1975). The electrostatic interactions and the thermal effects were omitted. The initial atomic coordinates were taken from the final refinement of the X-ray structure. The two-positional disorder of O(33) was neglected; only O(133) was retained with unit-weight contribution. A single guest enantiomer was included in the host lattice, which was arbitrarily built of (M)-(−)-TOT molecules. The packing energies with the guest R and S configurations are −330·5 and −328·2 kJ mol^{-1}, respectively, when the cell parameters are held fixed. With relaxation of the latter, the corresponding lattice energies · drop to −336·2 and −331·7 kJ mol^{-1}, respectively. Differences between observed and calculated cell constants remain small as demonstrated by the calculated values $a = 13·350$, $c = 29·734$ Å with the guest R configuration; and $a = 13·367$, $c = 29·895$ Å with the S configuration. This means that the applied potentials reproduce satisfactorily the interaction energies at both short and long distances. Similar calculations with fixed cell parameters, but including the global minimum energy R conformation of the guest, place the lattice energy about 50% higher than that calculated with the more strained guest molecule, thus corroborating the conformation of (2) derived from the X-ray diffraction data.

Host–guest correlation of configuration. The diastereomeric host–guest interaction is expressed by the difference between the lattice energies of the clathrates accommodating the R and S configurations, respectively. The significance of the magnitude of this energy difference in relation to the clathrate enantioselectivity has been discussed elsewhere (Gerdil & Allemand, 1980; Gerdil, 1987). In the present case, the

calculated lattice energies favour the diastereomeric aggregate (M)-(−)-TOT/(R)-2 by about 2–3 kJ mol^{-1}, a value that points to a low chiral recognition for the guest molecule.

Upon dissolution of a single clathrate crystal, the TOT molecules racemize and a measurable residual optical activity of the solution might result from an enantiomeric excess (e.e.) of the guest. A weak, but significant, residual negative rotation was measured with (M)-(−)-TOT/2, whereas the opposite complementary rotation was measured with (P)-(+)-TOT/2. An estimation of the e.e. and the configuration of the preferred enantiomer were deduced from the known $[\alpha]_D$ of (S)-(2): +33·7° (Kenyon & Snellgrove, 1925; Brown & Ganesh Pai, 1985). From the amplitude of the optical rotations the e.e. was estimated at 4–6%. Both the observed low chiral recognition and preferred configuration are in agreement with the semi-empirical calculations mentioned above. These results receive additional support in a former study revealing a remarkable correlation between the configuration of TOT in a single clathrate crystal and the configuration of sterically comparable guests (Arad-Yellin, Green, Knossow & Tsoucaris, 1983; Gerdil, 1987). In the present case, (R)-(2), which is isosteric with (R)-2-butanol, is expected to be correlated with (M)-TOT, as was experimentally verified.

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