Tri-O-thymotide / (R)-2-butanol (2:1) clathrate $C_{33}H_{36}O_6 \cdot {}^1/_2C_4H_{10}O$

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TRI-O-THYMOTIDE / (R)-2-BUTANOL (2:1) CLATHRATE

$C_{33}H_{36}O_6 \cdot \frac{1}{2} C_4H_{10}O$

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Introduction. The determination of the absolute conformation of tri-o-thymotide (TOT) by optical rotation and crystal structure analysis of the clathrate with (R)-2-butanol has recently been reported (R. Gerdil & J. Allemand, 1979). Detailed information is now presented of the X-ray structure analysis of the clathrate and of some of its relevant structural features.

Crystal data. $C_{33}H_{36}O_6 \cdot \frac{1}{2} C_4H_{10}O$; space group $P3_121$. Lattice parameters at 298°K : a = 13.598(3), c = 30.447(8) Å; at 123°K : a = 13.442(9), c = 30.10(3) Å. Z = 6 ; D_m = 1.149 ; D_x = 1.156 g cm^{-3}.

Intensity data, structure determination and refinement. Crystals were grown from optically pure (R)-2-butanol. Lattice parameters and diffracted intensities were measured at 123°K on a four-circle Philips PW 1100 diffractometer (graphite monochromator, MoKα radiation) using the ω-2θ technique. Of the 2921 reflections measured in the range $3^\circ < \theta < 20^\circ$, 2809 were

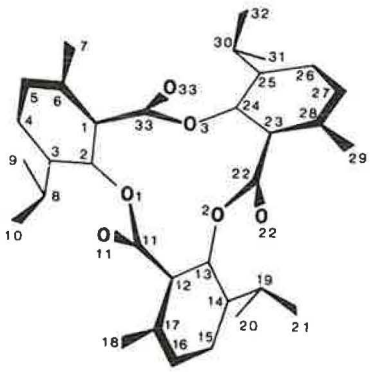
Fractional atomic coordinates of TOT (×10^4 *for non-hydrogen atoms and* ×10^3 *for hydrogen atoms*).

Atom	x	y	z	Atom	x	y	z
O(1)	9799(5)	3300(5)	-1054(2)	H(4)	1094(7)	125(7)	-187(3)
O(2)	8784(5)	4627(5)	-930(2)	H(5)	929(7)	39(7)	-229(3)
O(3)	8137(5)	3386(5)	-1717(2)	H1(7)	677(12)	46(12)	-206(4)
O(11)	8907(6)	2021(7)	-502(2)	H2(7)	745(11)	122(11)	-254(4)
O(22)	7133(6)	3813(7)	-549(2)	H3(7)	745(9)	3(9)	-245(3)
O(33)	6935(6)	1775(7)	-1359(3)	H(8)	1152(15)	331(15)	-93(6)
C(1)	8706(8)	2007(8)	-1632(3)	H1(9)	1287(9)	272(9)	-153(3)
C(2)	9669(8)	2475(8)	-1360(3)	H2(9)	1289(10)	392(10)	-163(4)
C(3)	10542(9)	2224(8)	-1430(3)	H3(9)	1333(10)	357(10)	-112(4)
C(4)	10405(8)	1488(9)	-1769(3)	H1(10)	1085(9)	163(8)	-60(3)
C(5)	9445(10)	1021(9)	-2049(4)	H2(10)	1138(10)	99(10)	-94(4)
C(6)	8562(8)	1266(8)	-1975(3)	H3(10)	1213(8)	204(8)	-66(3)
C(7)	7493(10)	707(10)	-2267(4)	H(15)	1075(10)	687(10)	24(4)
C(8)	11584(9)	2712(8)	-1123(3)	H(16)	1118(10)	559(10)	43(4)
C(9)	12692(9)	3224(10)	-1386(4)	H1(18)	1004(10)	270(11)	29(4)
C(10)	11490(9)	1764(11)	-807(4)	H2(18)	1109(10)	315(10)	-1(4)
C(11)	9379(8)	2977(9)	-640(3)	H3(18)	1131(11)	390(11)	42(4)
C(12)	9681(7)	4036(8)	-374(2)	H(19)	901(11)	655(10)	-79(4)
C(13)	9400(7)	4841(8)	-534(3)	H1(20)	1104(10)	807(10)	-32(4)
C(14)	9757(8)	5894(9)	-324(3)	H2(20)	1105(12)	759(13)	-89(5)
C(15)	10435(8)	6128(8)	49(3)	H3(20)	1052(10)	847(10)	-78(4)
C(16)	10700(8)	5327(8)	222(3)	H1(21)	810(10)	638(10)	-9(4)
C(17)	10341(7)	4283(8)	11(3)	H2(21)	928(8)	747(8)	8(3)
C(18)	10704(9)	3446(8)	193(3)	H3(21)	851(8)	760(8)	-37(3)
C(19)	9478(8)	6775(8)	-512(3)	H(26)	561(9)	416(9)	-242(3)
C(20)	10600(10)	7871(9)	-650(3)	H(27)	522(12)	489(12)	-183(4)
C(21)	8803(11)	7075(10)	-178(3)	H1(29)	562(9)	440(9)	-80(3)
C(22)	7615(8)	4141(8)	-893(3)	H2(29)	682(9)	567(9)	-77(4)
C(23)	7066(8)	4145(7)	-1325(3)	H3(29)	560(11)	537(11)	-102(4)
C(24)	7317(7)	3768(7)	-1712(3)	H(30)	770(8)	301(8)	-245(3)
C(25)	6823(7)	3758(7)	-2123(3)	H1(31)	719(8)	455(7)	-294(3)
C(26)	6052(8)	4163(8)	-2126(3)	H2(31)	854(12)	508(12)	-279(4)
C(27)	5803(8)	4570(8)	-1737(3)	H3(31)	780(8)	395(9)	-310(3)
C(28)	6306(8)	4562(7)	-1338(3)	H1(32)	564(7)	173(7)	-253(3)
C(29)	6014(9)	5013(9)	-922(4)	H2(32)	553(8)	276(9)	-287(3)
C(30)	7088(8)	3317(8)	-2540(2)	H3(32)	610(11)	192(11)	-301(4)
C(31)	7440(9)	4315(8)	-2876(3)				
C(32)	5999(9)	2352(8)	-2748(3)				
C(33)	7801(8)	2336(8)	-1543(3)				

considered observed at the $2\sigma_F$ level and with $[F_o] > 8$. The structure was solved by direct methods in space group $P3_1$, using the XRAY system adaptation of the MULTAN multiple solution program (1976). At the end of the initial isotropic refinement, a different synthesis revealed a total of 22 H atoms of either one of the TOT molecules of the asymmetric unit. The positions of the remaining H atoms were calculated. A peak analysis of the contents of the cavity allowed the recognition of the molecular configuration of the guest molecule; however the structure model arrived at displayed unsatisfactory bond distances which did not considerably improve after two further cycles of refinement. Therefore a minimum energy conformation for 2-butanol was calculated using empirical force field methods (Kao & Allinger, 1977). The resulting structure, though still consistent with the initial X-ray model, had bond distances and angles within the expected ranges and provided, in addition, a set of internal values for the H atom positions. The position of the rigid model within the cage, was subsequently refined alternately with the TOT parameters by block-diagonal least-squares procedures. At a later stage of the refinement, an examination of the electron density within the cage showed indications of a statistical two-fold disorder of the guest molecule consistent with space group $P3_121$. Therefore refinement was also carried out in this space group using a statistical weight of 1/2 for each equivalent position of the guest molecule. Anisotropic (resp. isotropic) temperature

Bond distances (Å) *and atom-numbering system for the* TOT *molecule.*

O(1) -C(2)	1.384(13)	C(12)-C(13)	1.398(17)
O(1) -C(11)	1.348(12)	C(12)-C(17)	1.396(12)
O(2) -C(13)	1.397(10)	C(13)-C(14)	1.397(10)
O(2) -C(22)	1.373(11)	C(14)-C(15)	1.380(13)
O(3) -C(24)	1.429(15)	C(14)-C(19)	1.519(18)
O(3) -C(33)	1.355(13)	C(15)-C(16)	1.394(18)
O(11)-C(11)	1.188(13)	C(16)-C(17)	1.389(14)
O(22)-C(22)	1.181(10)	C(17)-C(18)	1.533(18)
O(33)-C(33)	1.163(12)	C(19)-C(20)	1.547(12)
C(1) -C(2)	1.388(14)	C(19)-C(21)	1.538(19)
C(1) -C(6)	1.380(14)	C(22)-C(23)	1.497(14)
C(1) -C(33)	1.512(18)	C(23)-C(24)	1.376(14)
C(2) -C(3)	1.389(19)	C(23)-C(28)	1.391(18)
C(3) -C(4)	1.369(15)	C(24)-C(25)	1.401(12)
C(3) -C(8)	1.525(14)	C(25)-C(26)	1.391(18)
C(4) -C(5)	1.399(15)	C(25)-C(30)	1.506(13)
C(5) -C(6)	1.399(20)	C(26)-C(27)	1.401(15)
C(6) -C(7)	1.523(14)	C(27)-C(28)	1.381(14)
C(8) -C(9)	1.514(15)	C(28)-C(29)	1.526(16)
C(8) -C(10)	1.544(18)	C(30)-C(31)	1.554(12)
C(11)-C(12)	1.500(15)	C(30)-C(32)	1.524(11)



Bond angles (deg) *of* TOT.

C(2) -O(1) -C(11)	119.6(8)	C(14)-C(15)-C(16)	121.5(9)
C(13)-O(2) -C(22)	116.6(6)	C(15)-C(16)-C(17)	121.1(8)
C(24)-O(3) -C(33)	117.0(7)	C(12)-C(17)-C(16)	118.6(11)
C(2) -C(1) -C(6)	122.1(12)	C(12)-C(17)-C(18)	121.3(9)
C(2) -C(1) -C(33)	117.9(9)	C(16)-C(17)-C(18)	120.1(8)
C(6) -C(1) -C(33)	120.1(9)	C(14)-C(19)-C(20)	109.8(10)
O(1) -C(2) -C(1)	118.1(11)	C(14)-C(19)-C(21)	111.8(8)
O(1) -C(2) -C(3)	120.7(8)	C(20)-C(19)-C(21)	110.3(9)
C(1) -C(2) -C(3)	120.7(10)	O(2) -C(22)-O(22)	122.2(8)
C(2) -C(3) -C(4)	117.6(9)	O(2) -C(22)-C(23)	112.1(7)
C(2) -C(3) -C(8)	120.7(9)	O(22)-C(22)-C(23)	125.7(9)
C(4) -C(3) -C(8)	121.6(12)	O(22)-C(23)-C(24)	121.5(11)
C(3) -C(4) -C(5)	122.2(13)	C(22)-C(23)-C(28)	119.2(9)
C(4) -C(5) -C(6)	120.0(11)	C(24)-C(23)-C(28)	119.3(9)
C(1) -C(6) -C(5)	117.3(9)	O(3) -C(24)-C(23)	121.1(8)
C(1) -C(6) -C(7)	123.0(12)	O(3) -C(24)-C(25)	115.7(8)
C(5) -C(6) -C(7)	119.8(10)	C(23)-C(24)-C(25)	123.2(11)
C(3) -C(8) -C(9)	111.2(8)	C(24)-C(25)-C(26)	116.5(9)
C(3) -C(8) -C(10)	109.9(7)	C(24)-C(25)-C(30)	122.4(10)
C(9) -C(8) -C(10)	110.7(11)	C(26)-C(25)-C(30)	121.2(8)
O(1) -C(11)-O(11)	125.6(11)	C(25)-C(26)-C(27)	121.1(9)
O(1) -C(11)-C(12)	108.4(8)	C(26)-C(27)-C(28)	120.6(12)
O(11)-C(11)-C(12)	125.9(9)	C(23)-C(28)-C(27)	119.3(10)
C(11)-C(12)-C(13)	120.1(8)	C(23)-C(28)-C(29)	121.6(9)
C(11)-C(12)-C(17)	120.5(11)	C(27)-C(28)-C(29)	119.1(11)
C(13)-C(12)-C(17)	119.1(9)	C(25)-C(30)-C(31)	110.2(8)
O(2) -C(13)-C(12)	119.7(8)	C(25)-C(30)-C(32)	111.3(8)
O(2) -C(13)-C(14)	117.5(10)	C(31)-C(30)-C(32)	110.7(7)
C(12)-C(13)-C(14)	122.7(8)	O(3) -C(33)-O(33)	124.4(12)
C(13)-C(14)-C(15)	116.9(11)	O(3) -C(33)-C(1)	109.8(7)
C(13)-C(14)-C(19)	121.9(8)	O(33)-C(33)-C(1)	125.8(11)
C(15)-C(14)-C(19)	121.2(9)		

factors for the non-hydrogen atoms (resp. H atoms) of TOT were included in the model during the latter stages of the refinement. An overall isotropic temperature factor was assigned to the atoms of 2-butanol ; its mean end-value was about three times larger than that found for TOT. At convergence the value $R_w = (\Sigma\, w\Delta^2/wF_o^2)^{1/2}$ was 0.068 with $P3_121$ (502 variables) and 0.080 with $P3_1$ (996 variables), with w = 1 for all reflections. The parameters reported in the Tables refer to data collected at 123°K.

Comments. The clathrate is of the cage type and the enclosed component is hold by six surrounding TOT molecules as shown in Fig. 1. Only van der Waals interactions contribute to stability. The 2-butanol molecule assumes a particular position within the cage: its central bond is approximately bisected by the crystallographic two-fold axis, so that by a rotation of 180° new positions for the methyl groups are obtained, which are experimentally indistinguishable from the original ones. In addition, the hydroxyl O atom is only shifted by 0.2 Å from the two-fold axis, therefore only an average position is observed, characterized by an elongated electron density in a direction approximately perpendicular to the C-O bond. No sign of a localized disorder in any of the atomic positions of the TOT was noticed.

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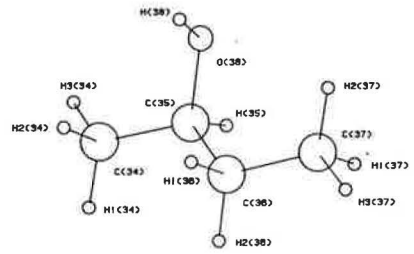
Fractional atomic coordinates of (R)-2-butanol ($\times 10^4$) *and atom numbering system.*

Atom	x	y	z	Atom	x	y	z
C(34)	2703	-1449	-195	H(35)	3401	308	-219
C(35)	3111	-194	-187	H1(36)	3583	-187	-119
C(36)	3977	307	-150	H2(36)	4719	200	-158
C(37)	4360	1567	-143	H1(37)	4755	2077	-173
O(38)	2173	-53	-175	H2(37)	3661	1709	-132
H1(34)	3410	-1593	-204	H3(37)	4995	1953	-116
H2(34)	2288	-1938	-165	H(38)	1800	-350	-177
H3(34)	2054	-1801	-221				



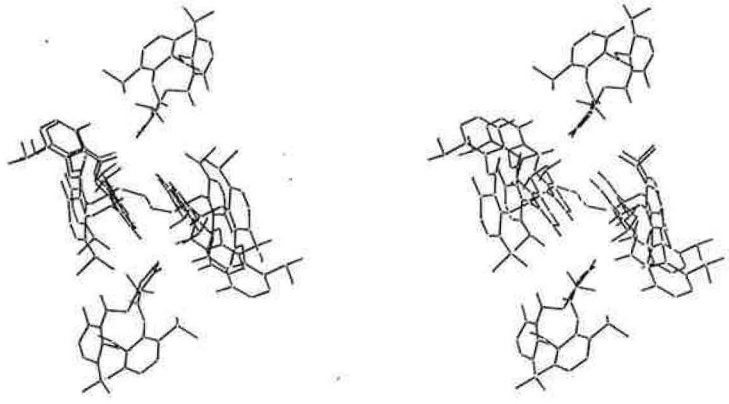


Fig. 1. Stereoscopic view of the cage down the crystallographic two-fold axis. The six (-)-tri-o-thymotide molecules in contac with (R)-2-butanol are shown.

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